DOPPLER ASSESSMENT OF FOETUS WITH IUGR

Dissertation submitted in partial fulfilment of the

Requirement for the award of the Degree of

M.S. DEGREE – BRANCH VI

OBSTETRICS AND GYNAECOLOGY

MAY 2018

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY,

CHENNAI,

TAMIL NADU

CERTIFICATE

This is to certify that the Dissertation entitled "**DOPPLER ASSESSMENT OF FOETUS WITH IUGR**" submitted by **Dr.N.SELVA ESAKKI, MBBS.,D.L.O.,** to The Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfilment for the award of M.S (Obstetrics and Gynaecology) is a bonafide work carried out by her under my guidance and supervision during the academic year 2015-2018. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the regulation for the award of M.S. Degree (Branch VI) in Obstetrics and Gynaecology.

It was not submitted to the award of any degree/diploma to any University either in part or in full previously.

Place: Tirunelveli.
Date:

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INSTITUTIONAL RESEARCH ETHICS COMMITTEE

CERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO:864/O&G/2016

PROTOCOL TITLE: DOPPLER ASSESMENT OF THE FETUS WITH INTRA UTERINE GROWTH RESTRICTION.

PRINCIPAL INVESTIGATOR: Dr. N. SELVA ESAKKI, MBBS, DLO.,

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE IN OBSTETRICS AND GYNAECOLOGY

DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear , Dr.N. Selva Esakki, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 05.08.2016.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1. TIREC Application Form ☐
2. Study Protocol ☐
3. Department Research Committee Approval ☐
4. Patient Information Document and Consent Form in English and Vernacular Language ☐
5. Investigator's Brochure ☐
6. Proposed Methods for Patient Accrual Proposed ☐
7. Curriculum Vitae of the Principal Investigator ☐
8. Insurance /Compensation Policy ☐
9. Investigator's Agreement with Sponsor ☐
10. Investigator's Undertaking ☐
11. DCGI/DGFT approval ☐
12. Clinical Trial Agreement (CTA) ☐
13. Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA) ☐
14. Clinical Trials Registry-India (CTRI) Registration ☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
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CERTIFICATE - II

This is certify that this dissertation work title **"DOPPLER ASSESSMENT OF FOETUS WITH IUGR"** of the candidate **Dr.N.SELVA ESAKKI,** with registration Number **221516353** for the award of M.S. in the branch of **OBSTETRICS AND GYNAECOLOGY.** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **13 percentage** of plagiarism in the dissertation.

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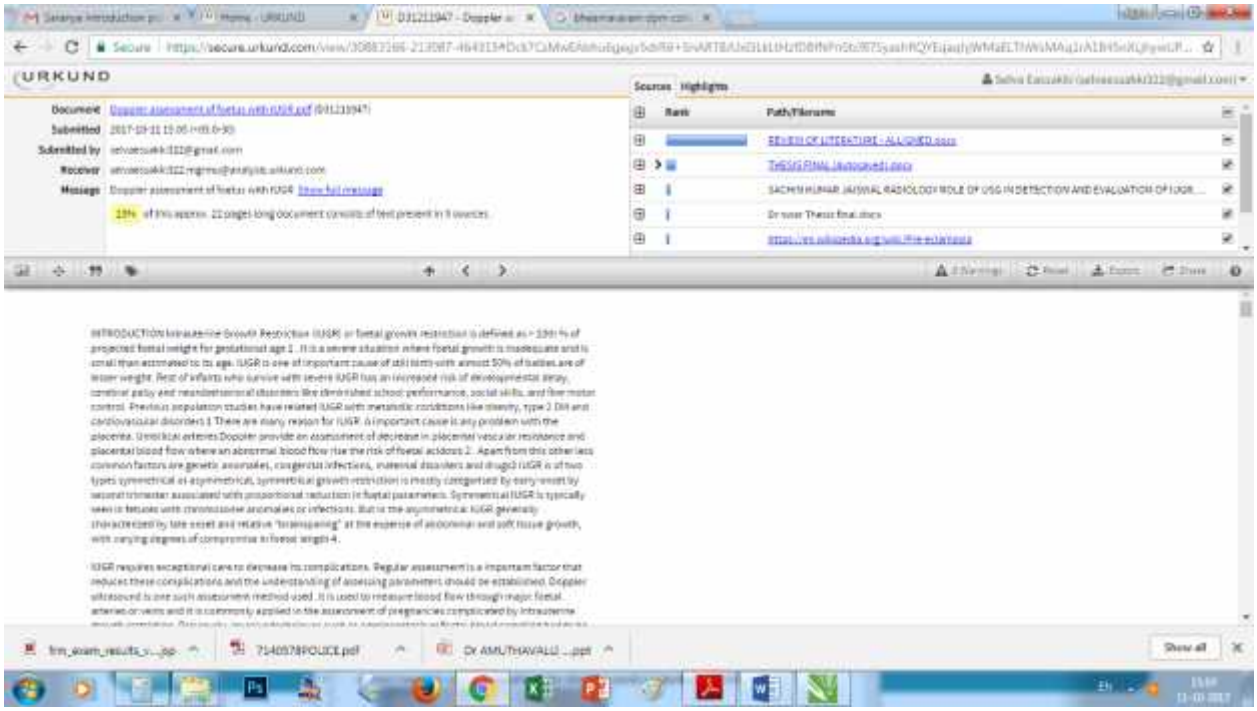
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SACHIN KUMAR JAISWAL RADIOLOGY ROLE OF USG IN DETECTION AND EVALUATION OF IUGR....
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INTRODUCTION Intrauterine Growth Restriction (IUGR) or foetal growth restriction is defined as < 10th % of projected foetal weight for gestational age 1 . It is a severe situation where foetal growth is inadequate and is small than estimated to its age. IUGR is one of important cause of still birth with almost 50% of babies are of lesser weight. Rest of infants who survive with severe IUGR has an increased risk of developmental delay, cerebral palsy and neurobehavioral disorders like diminished school performance, social skills, and fine motor control. Previous population studies have related IUGR with metabolic conditions like obesity, type 2 DM and cardiovascular disorders 1 There are many reason for IUGR. A important cause is any problem with the placenta. Umbilical arteries Doppler provide an assessment of decrease in placental vascular resistance and placental blood flow where an abnormal blood flow rise the risk of foetal acidosis 2. Apart from this other less common factors are genetic anomalies, congenital infections, maternal disorders and drugs3 IUGR is of two types symmetrical or asymmetrical, symmetrical growth restriction is mostly categorised by early onset by second trimester associated with proportional reduction in foetal parameters. Symmetrical IUGR is typically seen in fetuses with chromosome anomalies or infections. But in the asymmetrical IUGR generally characterized by late onset and relative "brainsparing" at the expense of abdominal and soft tissue growth, with varying degrees of compromise in foetal weight 4 .
IUGR requires exceptional care to decrease its complications. Regular assessment is a important factor that reduces these complications and the understanding of assessing parameters should be established. Doppler ultrasound is one such assessment method used . It is used to measure blood flow through major foetal arteries or veins and it is commonly applied in the assessment of pregnancies complicated by intrauterine
Show all

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INTRODUCTION

Intrauterine Growth Restriction (IUGR) or foetal growth restriction is defined as < 10th % of projected foetal weight for gestational age[1]. It is a severe situation where foetal growth is inadequate and is small than estimated to its age. IUGR is one of important cause of still birth with almost 50% of babies are of lesser weight. Rest of infants who survive with severe IUGR has an increased risk of developmental delay, cerebral palsy and neurobehavioral disorders like diminished school performance, social skills, and fine motor control. Previous population studies have related IUGR with metabolic conditions like obesity, type 2 DM and cardiovascular disorders[1]

There are many reason for IUGR. A important cause is any problem with the placenta. Umbilical arteries Doppler provide an assessment of decrease in placental vascular resistance and placental blood flow where an abnormal blood flow rise the risk of foetal acidosis[2]. Apart from this other less common factors are genetic anomalies, congenital infections, maternal disorders and drugs3

IUGR is of two types symmetrical or asymmetrical, symmetrical growth restriction is mostly categorised by early-onset by second trimester associated with proportional reduction in foetal parameters. Symmetrical IUGR is typically seen in fetuses with chromosome anomalies or infections. But in the asymmetrical IUGR generally characterized by late onset and relative “brainsparing” at the expense of abdominal and soft tissue growth, with varying degrees of compromise in foetal length[4].

IUGR requires exceptional care to decrease its complications. Regular assessment is a important factor that reduces these complications and the understanding of assessing parameters should be established.

Doppler ultrasound is one such assessment method used .It is used to measure blood flow through major foetal arteries or veins and it is commonly applied in the assessment of pregnancies complicated by intrauterine growth restriction. Previously, invasive techniques such as amniocentesis or foetal blood sampling had to be performed every few weeks in pregnancies with IUGR for severe foetal anaemia that could result in stillbirth .This novel and non-invasive approach has revolutionized monitoring of pregnancies with IUGR and has made invasive foetal testing for this indication generally unnecessary.[5].In Umbilical artery angle independent indices like pulsatility index or systolic/diastolic (S/D) ratio decrease with increasing gestational age because of a decreased placental vascular resistance and increase in end-diastolic velocity, which occurs physiologically. In pathologic conditions like IUGR fetuses, the EDF decreased due to blood shunting to vital organs (brain, heart), the umbilical artery wave-forms change and the angle-independent indices become abnormal with values above their reference ranges. These changes reflect an increased placental vascular resistance[5]. In this study we focus our measurements pulsatility index on foetal umbilical, middle-cerebral arteries and ductus venosus using doppler velocitometry because of their importance for detection of any abnormalities underlying IUGR.

AIM OF THE STUDY

To assess use of Doppler velocitometry of umbilical artery, middle cerebral artery and ductus venosus for non-anomalous foetus with suspected IUGR and to provide antepartum management of these pregnancies and in particular singleton pregnancy.

REVIEW OF LITERATURE

Intrauterine Growth Restriction (IUGR):

Intrauterine growth restriction is nothing but small for gestational age (SGA) foetuses where the foetus is smaller than estimated for the gestational age. The SGA also comprises fetuses which are constitutionally small and in fetuses whose growth has been constrained, most usually well-defined as a weight below the 10th percentile for the gestational age.[6-8]

At the end of pregnancy such IUGR babies end up with low birth weight. At least 60% of the 4 million neonatal mortality globally is related to low birth weight (LBW), which is mainly due to intrauterine growth restriction (IUGR), associated with preterm delivery, and genetic/chromosomal abnormalities, which further proves that under-nutrition is a leading health problem at birth.

The difference between a small baby and intrauterine growth restriction is based on physical criteria like skin texture and thickness, creases on soles of feet, firmness of ears, and appearance of the genitals and neurological like posture or type of flexion of hands and feet.[8]

There will also be lot of medical problems during and after birth for such IUGR babies. Some premature new-borns have no problems and physically well-developed whereas few new-borns have immature lungs resulting in respiratory distress syndrome, other findings like jaundice due to immaturity of liver function, and apnea an irregular breathing form due to an immature nervous system. Also these IUGR babies may manifest with low blood sugar (hypoglycemia), low blood calcium (hypocalcemia), polycythemia, and

swallowing of fluid from the amniotic sac during labor (meconium aspiration). Such neonates must be observed meticulously for signs of reduced oxygen supply, neonatal sepsis and particularly hypothermia which happens in IUGR infant due to diminished fat tissue which would help hold the infant's body temperature.[9]

Figure: The image above shows a normally-grown baby (right) and a growth-restricted baby (left).

General causes of intrauterine growth restriction (IUGR):

If the cause of IUGR is extrinsic to the fetus like maternal or uteroplacental then there will be decrease in transfer of oxygen and nutrients to the fetus. Due to this there will be reduced stores of glycogen and lipids in fetus. Hypoglycaemia at birth happened due to this reason. Whereas Polycythaemia happens due to rise in erythropoietin production influenced by chronic hypoxemia. Other features like hypothermia, thrombocytopenia, leukopenia,

hypocalcaemia are mostly due to IUGR. If the cause of IUGR is intrinsic to the fetus, growth is restricted due to genetic factors or as a sequela of infection.[9]

Hypertension complicates roughly 9% of all pregnancies with preeclampsia and in severe preeclampsia utero-placental perfusion is generally reduced and this results in high incidence of IUGR, foetal hypoxia and prenatal death[10].

After recognising a fetus with IUGR, an perfect and detailed history and physical examination are the most important tools for differentiating foetal from maternal and placental reasons and to plan antepartum management and improve foetal outcomes

Causes of IUGR

Maternal causes:

- Pre-pregnancy weight and nutritional status
- Poor weight gain during pregnancy
- Poor nutrition
- Anaemia
- Maternal smoking
- Recent pregnancy
- Pre-gestational and gestational diabetes
- Pulmonary,renal and cardiovascular disease
- Hypertension

Uteroplacental causes:

- Preeclampsia
- Multipara
- Uterine malformations
- Placental insufficiency

2.4.6.3 Foetal causes:

- Chromosomal abnormalities
- Vertically transmitted infections from mother

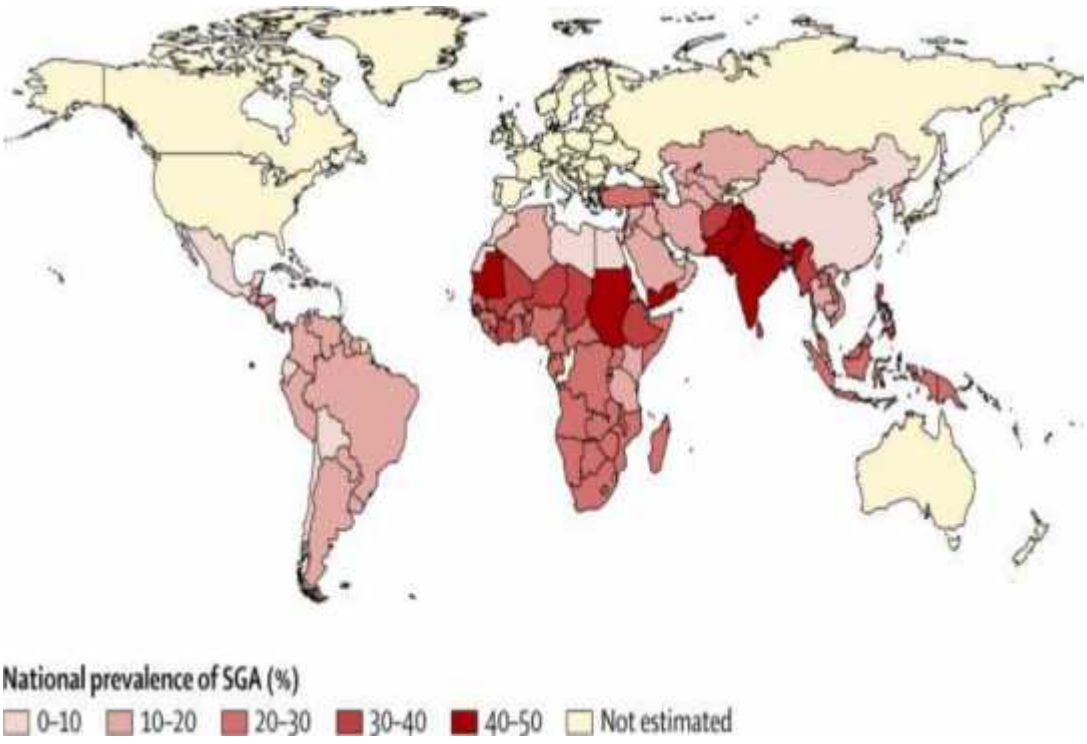


Figure: Distribution of small for gestational age (SGA) in the world

Classification OF IUGR:

There are 2 major types of IUGR:

- Symmetrical and
- Asymmetrical.

Some foetal and maternal conditions are related with both symmetrical and asymmetrical growth restriction[9] Asymmetrical IUGR is very common (70%). In asymmetrical IUGR, there is reduction of weight along with length. The head continues to grow at normal or near-normal rates (head sparing type). Absence of subcutaneous fat causes thin and small body out of proportion with the head. This may be a natural protective mechanism happened to promote brain development. In these neonates, the foetus would have grown routinely for the first two trimesters but come across problems in the third, sometimes due to complications such as pre-eclampsia. Apart from this there will be signs like dry, peeling skin and an overly-thin umbilical cord. These neonates have a high risk of hypoxia and hypoglycaemia. Asymmetrical IUGR is most frequently triggered by extrinsic issues that affect the foetus at latter part of gestation. Such causes are:

- Chronic elevated blood pressure.
- Severe malnutrition
- Genetic mutations and
- Ehlers–Danlos syndrome.[9]

Symmetrical IUGR is less common than asymmetrical type (20-25%). It is usually called as global growth restriction, and specifies that the foetus has underdeveloped throughout the duration of pregnancy and neonate is affected from a very early stage whereas it’s at later stages in asymmetrical IUGR. The

head circumference of neonate born with symmetrical IUGR is in proportion to the rest of the body. Common causes include:

- Early intrauterine infections, such as CMV infection, rubella or toxoplasmosis.
- Chromosomal abnormalities
- Anaemia
- Maternal substance abuse.[9]

Table 2.8: Classification OF IUGR

Symmetric	Asymmetric
20-30% of IUGR	70-80% of IUGR
Usually occurs early in pregnancy	Usually occurs later in pregnancy (3rd trimester)
Head circumference, length, and weight are decreased proportionally	Head circumference is spared relative to decreased weight, length, and/or abdominal circumference
Thought to result from an intrinsic (i.e. genetic) or first-trimester insult (e.g. infection) that interferes with early fetal cellular hyperplasia, producing uniformly reduced growth	Thought to result from adaptation to a hostile environment by redistributing blood flow in favour of vital organs (e.g. brain, heart) at the expense of nonvital fetal organs (e.g. liver, kidneys)

Diagnosis of IUGR:

For an exact diagnosis of IUGR one of important requirement is correct calculation of gestational age[11]. Taking into account that dates can be assessed from LMP or early first trimester ultrasound, the methods to diagnose IUGR are as follows, by using the ultrasound imaging techniques and Doppler imaging studies. There are signs and symptoms of IUGR such as

- Poor maternal weight gain
- Development of hypertension.
- Reduced foetal activity
- Small-for-dates pregnancy (determined by the symphysis-fundal height, SFH).

Normal pregnancies progress at 1cm/week, so 30cm at 30 weeks. Any SFH that is 3cm or more behind dates requires ultrasound investigations. Following tests should be done:

Ultrasound scans

Ultrasound scanning methods are nowadays used to observe foetal growth and analyse foetal biometry. USG is very much helpful in estimation of foetal weight and measurement of body parts like abdominal circumference, head circumference. Doppler studies of the foetal, placental and uterine vasculature were been in use since 1980's and have become important technique in assessing IUGR. USG and Doppler use a non-invasive ultrasound method, based on the Doppler principle. They evaluate the velocities of RBC flow within arteries. In the umbilical artery, if there is increase in ratios of the systolic/diastolic

frequency it reveals a growing quantity of impedance to blood flow in the placenta. This happens due to rise in placental circulatory resistance as a result of decrease in number of tertiary villous arteries, which mainly takes place due to maternal vascular disease such as hypertension.[12] Reduction in diastolic flow, absent diastolic flow or reversed diastolic flow during a cardiac cycle are signs of deteriorating IUGR.

Estimated foetal weight (EFW)

The EFW is assessed by quantifying the bi-parietal diameter (BPD) and head circumference (HC) of the baby's cranium, abdominal circumference (AC), and femur length (FL) on ultrasound. The average sizes are used as a reference range to decide if the developing foetus is too small to its gestational age. If the foetus is below the 10th percentile, then it is defined as small-for-gestational age *(*SGA*)* and a part of these foetus will be found to have true IUGR.

Doppler studies

Doppler studies are mainly useful in evaluating the blood flow to the foetuses**.** Early-onset IUGR pregnancies (typically found <32 weeks' gestation) have increased blood flow resistance in the umbilical arteries. Also there may be:

- Brain redistribution*:* abnormal flow in the baby's brain characterized by augmented flow in the middle cerebral artery or MCA;
- Anomalous flow in the ductus venousus;
- Utero-placental vascular insufficiency:

In contrast, in the late-onset IUGR (found after 36 weeks), the uterine and umbilical artery Doppler studies are mostly normal. However, late onset-IUGR babies mostly have abnormal middle cerebral artery (MCA) Doppler[13, 14] (Scott and Usher, Lubo)

Morbidity and mortality of IUGR:

The risk of morbidity and mortality depends on basic pathology which mainly caused the growth problem, severity of growth restriction, gestational age of mother –how much earlier it is, and the baby's gestational age at birth. The 10th percentile is commonly used to define "small for gestational age" at all stages of pregnancy. The risk of neonatal mortality at the 10th percentile has a bimodal distribution with higher mortality at 26 and 34 weeks' of gestation. There is a spurt in mortality and neonatal problems as the foetal weight decreases below the 5th percentile. IUGR is a feature commonly seen in approximately 50% of all stillbirths. Also the higher incidence of both short-term and long-term sequlae is higher for growth-restricted babies delivered prematurely .Normal labour will be difficult to tolerate and mostly babies are delivered by caesarean section. After birth these infants have high chances of having problems like hypoglycaemia, neonatal sepsis, hypothermia and polycythaemia. Also they are more prone to jaundice and meconium aspiration syndrome. [15]

Those infants who survive severe IUGR have in increased risk of morbidity like long-term developmental delay and neuromotor disabilities such as cerebral palsy.

Repeated abdominal circumference or foetal weight assessments are the best screening tests for IUGR. Doppler studies are the gold standard for diagnosis and management. Where as complicated cases of early onset IUGR (< 30 weeks' gestation) may need a multi-vessel Doppler scan to evaluate pre-load, as well as after-load, also presence of severe intrauterine growth restriction.

Many a steps needed to be taken like

- Correct dates should be confirmed
- Is the developing baby is genuinely smaller than average
- Review of maternal and pregnancy risk factors for abnormal placental function
- Investigate non-placental causes of IUGR
- If there is no evidence of non-placental causes of IUGR, placental function testing is performed
- A plan of serial monitoring is then developed and Pediatric consultation before delivery[16].

Approach to IUGR:

Exact dating of the pregnancy is must! Dating is assessed based on the last menstrual period (LMP) using Nägele's rule (EDD = LMP + 9 months 7 days). If the dating of the pregnancy is in doubtful , the gestational age can also be evaluated by 1st trimester ultrasound measurement of the crown-rump length (CRL). If these values differ from normal reference ranges by more than 7 days,

then continuous ultrasound measurements are done every 2-4 weeks to assess the dates and estimate the foetal growth.

Generally screening for IUGR depends on symphysis-fundal height measurements which is done as a part of regular antenatal care[17]

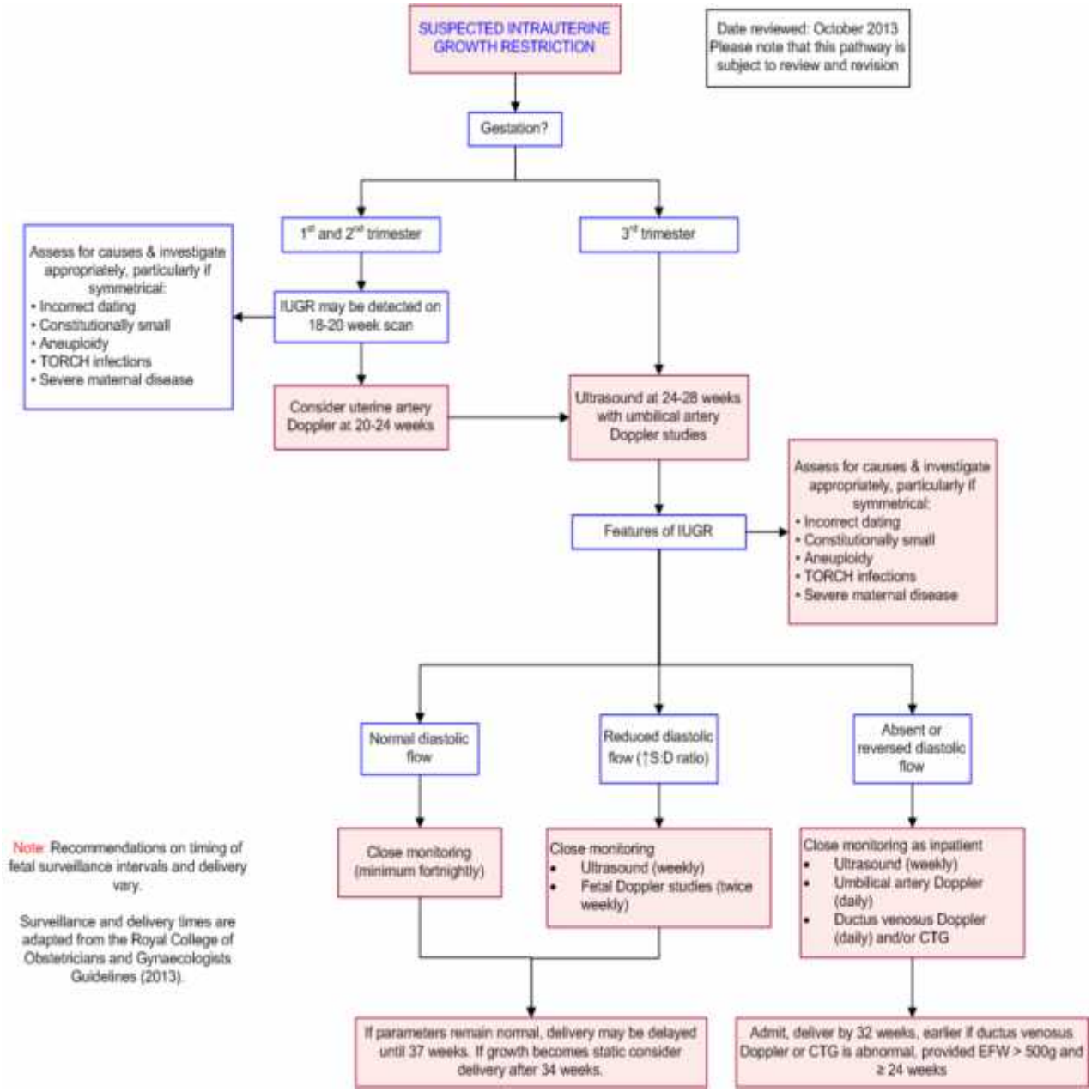


Figure 30: the intrauterine management of IUGR

Outcomes and clinical significance:

IUGR is present in 3-10% of pregnancies. Among stillborn infants 20% have IUGR. Infants with IUGR have a 4-8 times higher risk of perinatal mortality and almost of half of surviving babies with IUGR have some sort of morbidity. Eventually, the most important facets of IUGR are the cerebral or other neurological developmental outcomes, including learning disabilities. This outcome depends on the basic cause of IUGR. Hence only by confirming the cause of IUGR next probable plan of action is decision for every child[18]

The below investigation helps us in that direction such as

- Repeated assessments of blood flow velocity in foetal vessels using Doppler ultrasound.
- Absent or reversed end diastolic flow in the umbilical artery suggests the fetus is in poor condition.
- Non-stress test
- Biophysical profile
- Repeated foetal weight assessments
- Amniotic fluid volume
- A detailed foetal anatomic survey by ultrasound

Other studies, such as testing for congenital infections or karyotyping are decided on an individual basis. After this if needed course of antepartum steroids is advised for preterm foetuses to improve lung maturation.[18]

IUGR infants born preterm has an higher risk of complications medically as compared to term neonates. In terms of growth some IUGR babies do draw level and become average-sized children and adults. The pattern for this catch-up growth is mostly seen during the first year of life[19].

Treatment

No effective therapies for IUGR available

Hyperoxygenation

Nicolaides et al and Battagia et al found decrease in foetal mortality when mother is exposed to oxygen.[20]

Aspirin

Aspirin inhibits thromboxane A 2 and converts thromboxane to prostacycline. It causes vasodilation in uteroplacental circulation and hence decrease the incidence of IUGR and preeclampsia.

Optimal time of delivery

- IUGR foetus are chronically hypoxemic. Continued intrauterine hypoxia leads to metabolic deterioration.
- Foetus should be delivered if the risk of foetal death increases. ACOG (2000)
- A fine balance needs to be made between prematurity and intrauterine hypoxia (GRI Study – 2003)

Determinates of timing of delivery of IUGR fetus

- Aetiology of IUGR
- Biophysical profile
- Non stress test (NST)
- Foetal movement
- Amniotic fluid index
- Doppler velocimetry
- Interval growth
- Gestational age
- Maternal co – morbidities

Management based on gestational age:

Before 26 weeks:

- Outcome is very poor because of extreme prematurity and IUGR.
- Delivery is indicated only for maternal indications like severe preeclampsia.
- Survival rate is less than 50% and the long term handicap is around 30-50%
- Option of non-intervention and probable IUD should be given in the absence of maternal disease and risk.

26-28 weeks

- Administer steroids to enhance lung maturity.

- Monitor foetus for signs of worsening hypoxia
- Decision to deliver depends on the type of intensive care for these babies.

28-31 weeks

- Risk of perinatal mortality is high due to prematurity, Doppler studies of the ductus venosus may be used to assist in decision making.
- Normal flow in ductus venosus may allow extension of pregnancy to 32-34 weeks if other tests of wellbeing remain normal.
- Administer two doses of steroids before delivery.

32- 36 weeks

- Risk of respiratory distress syndrome is reduced
- A primary factor that should be considered after 34 weeks of gestation is the risk of foetal death, late onset IUGR contributes of >50% of unanticipated stillbirths at term.

>36 weeks

- Consider delivery in IUGR with oligohydramnios >36 Weeks
- Induction of labour with careful foetal monitoring is important as these foetuses will not tolerate acute hypoxia.

Mode of delivery

Due to increased prevalence of chronic hypoxia and oligohydramnios among IUGR, the rate of caesarean section will increase.

Indications for caesarean section

- Severe IUGR with EFW <1.5 Kg
- Preterm IUGR <32 weeks
- Non –reassuring foetal heart rate
- Metabolic acidosis and
- Other obstetric indications.

During labour there should be continuous intrapartum foetal monitoring to detect any progressive hypoxia and to provide intensive neonatal care.

Recurrent risk for IUGR

Risk of IUGR in second pregnancy is 29% and the risk in third pregnancy rises to 44%. (Bakketeig and Hoffman, 1983).

Hypertensive disorders of pregnancy

Hypertensive disorders in pregnancy is one another important cause of maternal mortality globally. A pregnant mother diagnosed with hypertension have an increased danger of developing chronic hypertension and cardiovascular problems in later part of life. There is also increased risk to the baby in the form of still birth, preterm birth and IUGR.

Definitions

According to National High Blood Pressure Working group (NHEPEP) and ACOG, hypertension in pregnancy is defined as systolic BP >140mm of Hg

and diastolic BP >90mm of Hg in a previously normotensive women after 20 weeks of gestation on two occasions 4-6 hours apart.

Pre-eclampsia is one of important cause of maternal and perinatal mortality and morbidity globally causing about 24% of all maternal deaths in India.[32,33] There is a 5- times high risk of perinatal mortality in pre-eclampsia with associated prematurity.[34] The term gestational hypertension is used now to describe any form of new onset pregnancy related hypertension. It was adopted by the Working group of NHBPEP (2000), which proposed a classification system based on clinical simplicity to guide management.[35]

Accordingly there are four types of hypertensive disease:

1. Gestational Hypertension

2. Pre-eclampsia and eclampsia syndrome

3. Chronic hypertension

4. Pre-eclampsia superimposed on chronic hypertension

Diagnostic criteria of hypertensive disorders complicating pregnancy:

I. GESTATIONAL HYPERTENSION:

1. BP ≥ 140/90 mmHg noticed for the first time during pregnancy after 20 weeks in a previously normotensive pregnant mother.

2. No proteinuria

3. Blood pressure returns to normal after 12 weeks postpartum

4. Final diagnosis made only postpartum

5. May have other signs or symptoms of pre-eclampsia, for eg; epigastric discomfort or thrombocytopenia

II. PRE-ECLAMPSIA AND ECLAMPSIA:

A. Non- severe pre-eclampsia

1. BP ≥ 140/90 mmHg after 20 weeks' gestation systolic B.P < 160 mm Hg and diastolic B.P < 110mm Hg.

2. Proteinuria: None to positive

3. No symptoms / signs / laboratory features of severe PE.

Severe pre-eclampsia**:**

1. BP ≥ 160/110 mmHg

2. Proteinuria

3. Headache

4. Visual disturbances

5. Upper abdominal pain

6. Oliguria

7. Convulsion [Eclampsia]

8. Elevated Serum creatinine

9. Thrombocytopenia

10. Elevated Serum transaminase

11. Prominent Foetal growth restriction

12. Pulmonary oedema.

B. ECLAMPSIA:

Seizures that cannot be attributed to other causes in a woman with pre-eclampsia

III. CHRONIC HYPERTENSION:

1. BP ≥ 140/90 mmHg before pregnancy or diagnosed before 20 weeks' gestation not attributable to gestational trophoblastic disease

OR

2. Hypertension first confirmed after 20 weeks' gestation and persistent after 12 weeks' postpartum

IV. SUPERIMPOSED PRE-ECLAMPSIA (on Chronic Hypertension):

1. New – onset proteinuria ≥ 300 mg/2 hours in hypertensive women but no proteinuria before 20 weeks' gestation

2. A sudden increase in proteinuria or BP

3. Platelet count < 1,00,000/mm^3 in women with hypertension and proteinuria before 20 weeks' gestation.[35]

PROTEINURIA

15-25% of gestational hypertension progress to preeclampsia. Urine dipstick testing is performed on a fresh, clean voided, specimen before pelvic examination to detect proteinuria.

Results can be interpreted as follows

- Negative
- Trace
- 1+=between 30 and 100 mg/dl
- 2+= between 100 and 300 mg/dl
- 3+= between 300 and 1000 mg/dl
- 4+= >1000 mg/dl
- Proteinuria >2+ is significant
- Proteinuria>1 + should be followed by mid - stream urine culture to rule out infection and to check for significant proteinuria.
- 24- hr urine collection is the gold standard to quantify protein >=300mg/d in 24 hr urine collection is significant proteinuria. Now - a- days 24 hour test is replaced by spot urine protein creatinine ratio. (Durnwald and MERCER,)

Incidence rate of PIH

- 6-15 percent in Nullipara
- 2-4 percent in multipara.

❖ RISK FACTORS FOR PRE-ECLAMPSIA

The various risk factors for the development of gestational hypertension and PE are as follows.

❖ GENETIC FACTORS:

1. Genetic pre-disposition
2. Race and Ethnicity: more common in blacks and Asians.
3. Family history of Pre-eclampsia
4. Pregnancy by ovum donation

❖ AGE AND PARITY:

1. Teenage pregnancy
2. Age more than 40 years
3. Long interval between pregnancies
4. Nulliparity

❖ PARTNER RELATED FACTORS:

1. Change of partner
2. Partner who fathered a pre-eclamptic pregnancy in another woman
3. Limited sperm exposure
4. Pregnancy due to donor insemination

❖ PRESENCE OF UNDERLYING DISORDERS:

1. Chronic Hypertension
2. Diabetes Mellitus
3. Renal Disease
4. Obesity

5. Polycystic ovarian syndrome

6. Migraine

7. Collagen Vascular Disease

8. Factor 5 Leiden deficiency

9. Thrombophilia

10. Uncontrolled Hyperthyroidism

- PREGNANCY RELATED RISK FACTORS:

1. Multiple Pregnancy

2. Hydatidiform Mole

3. Hydrops Foetalis

4. Congenital and chromosomal foetal anomalies

- MISCELLANEOUS FACTORS:

1. Smoking (reduced risk)

2. Psychological strain and stress at working place

3. Previous history of pre-eclampsia.[47]

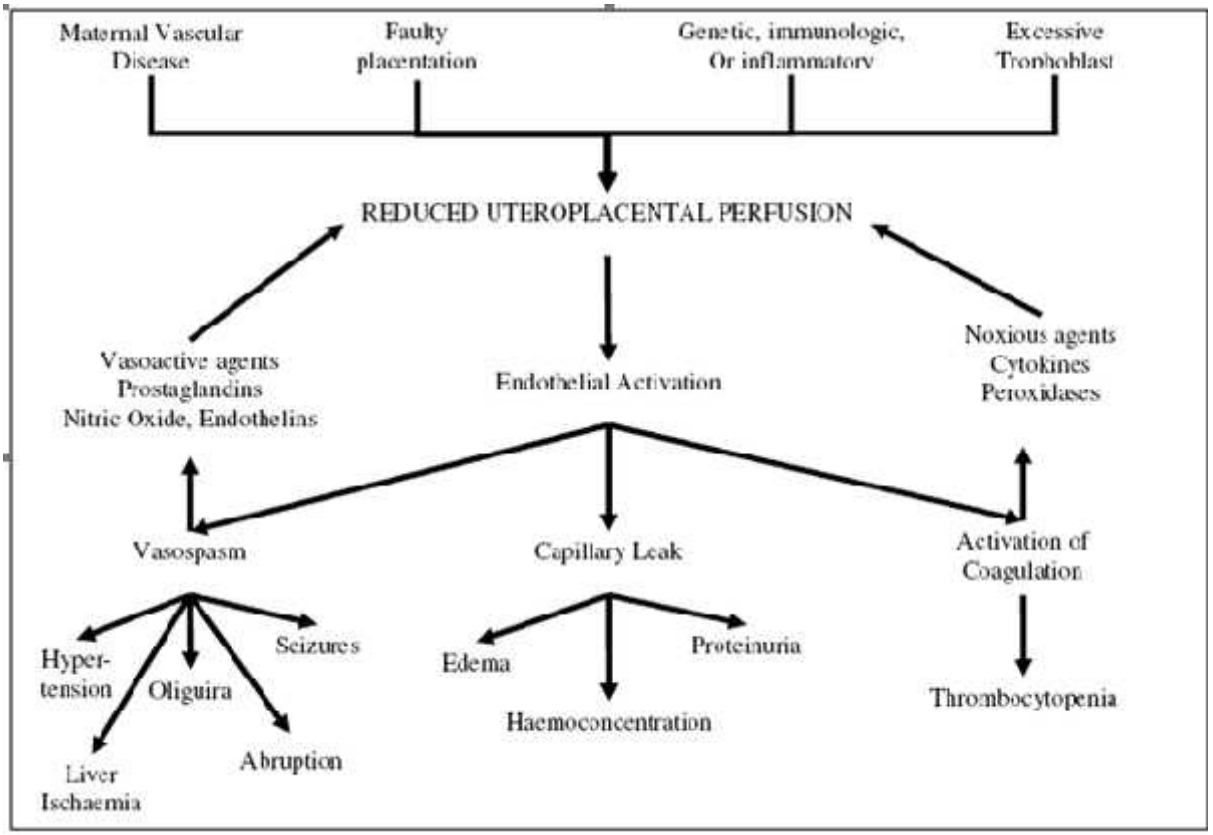


FIGURE: pathophysiological considerations in hypertensive disorders of pregnancy.[46]

PREVENTION OF PRE-ECLAMPSIA:

Prevention of pre-eclampsia is a great step in antenatal care.

PRIMARY PREVENTION:

Primary Prevention may be possible to some extent by the modification of some of the risk factors of pre-eclampsia. Prevention or effective treatment for obesity ends up in significant decrease in the frequency of pre-eclampsia and should be advised. Similarly, women with Diabetes, Chronic Hypertension, renal

and other medical disorders should have their primary condition under control before venturing into conception.[49]

SECONDARY PREVENTION:

Secondary prevention of any disease is feasible if the following 3 basic requirements are fulfilled and are available.[50]

1. Accurate knowledge of the patho-physiological mechanisms

2. Availability of effective screening methods

3. Means of intervention and modification of patho-physiology

Unfortunately, in-spite of extensive research world-wide, none of the three criteria are available for pre-eclampsia to make a strong case for successful secondary prevention. The multi-factorial origin of the disease suggests that it is highly unlikely that there will be a single predictive test available in future to predict PE.

Interventional methods:

A. Non-Pharmacological Interventions

B. Nutritional Interventions

C. Pharmacological Interventions

A. *Non-Pharmacological Interventions*

Life- Style Changes: Regular ante-natal care is mandatory for the prevention and early detection of PE. Job stress including lack of control over work place, timing and frequency of breaks may be related to various adverse events which also includes PE. Studies have shown positive correlation between high job stress and the risk of developing pre-eclampsia and gestational hypertension.[51]

Regular Physical Activity: Regular pre-natal exercise may prevent or decrease the progression of the disease as suggested by many previous studies.[52] the protective effect may be due to following mechanisms:

- Stimulation of placental growth and vascularity
- Reduction of oxidative stress
- Exercise induces reversal of maternal endothelial dysfunction

B. *NUTRITIONAL INTERVENTIONS*:

Dietary Protein and Energy Intake:

Many nutritional interventional studies have been proved to prevent pre-eclampsia including increasing protein and energy intake or restricting protein or energy intake for obese women. However, a recent overview of randomized trials of nutritional interventions during pregnancy reported no benefit of such measures in the prevention of pre-eclampsia.[53]

Fish Oils : Inclusion of fish oils in the diet, Eicosapentenoic acid and docosahexanoic acid, was shown by some studies to have a protective effect in the prevention of pre-eclampsia. They inhibit the synthesis of arachidonic acid.[54]

Alcohol Intake: There is no definite evidence that consumption of less than 120 gms of alcohol per week causes any adverse effects on pregnancy outcome including fetal growth, though there are some suggestions that excessive consumption of alcohol can aggravate or cause maternal hypertension.[55]

Arginine Supplementation: Few studies have documented that dietary supplementation with L-Arginine has been found to be useful in the prevention of pre-eclampsia.[56]

C. *PHARMACOLOGICAL INTERVENTIONS:*

Role of Antihypertensive drugs: It is well known fact that women with pre-existing chronic hypertension are at significantly increased risk of developing preeclampsia than their normotensive counterparts. The various anti-hypertensive medications like Methyldopa, Labetalol and Atenolol have been evaluated in various randomized trials for their efficacy in prevention of superimposed pre-eclampsia.[57] Critical analysis of all these trials failed to find any reduction in the incidence of pre-eclampsia.

Zinc Supplementation: Zinc concentration is decreased among women with hypertensive disease of pregnancy. Recent randomized clinical trials have failed to demonstrate the efficacy of zinc supplementation for the prevention of pre-eclampsia.[59]

Magnesium supplementation: Magnesium has a proven benefit for the prevention and treatment of severe pre-eclampsia and eclampsia. Hence it was first thought that deficiency of magnesium was important in the pathogenesis of pre-

eclampsia.[60] A Cochrane review of two trials could detect no apparent effect of magnesium supplementation on the prevention of pre-eclampsia.

Role of low dose aspirin: Low dose aspirin (50-150mg /day) therapy during pregnancy selectively inhibits platelet thromboxane-A2 biosynthesis with minimal effects on prostacyclin production.[61] Multiple clinical trials including the CLASP study established that the overall use of low dose aspirin in pregnant women was associated with a 12% decrease in the incidence of pre-eclampsia and 19% decrease in the pre-term delivery in the high risk group. Thus the only group in whom Low dose Aspirin may be justified are those especially at high risk for early onset pre-eclampsia.

Calcium Supplementation:

Data from epidemiological and observational studies have shown that there is an inverse relationship between calcium intake of 2 gms/day and the frequency of pre-eclampsia and eclampsia. This effect was greatest in women at high risk of hypertension and those with low baseline calcium intake.[64]

Before going in detail about Doppler velocimetry it's important to know the anatomy and physiology of the structures

Umbilical cord

The umbilical cord links the placenta with the ventral part of the embryo. It is a soft tortuous cord measuring about 50-60 cm long and 1 cm in diameter .It contains three umbilical vessels (one vein and two arteries) embedded in a

gelatinous material termed as Wharton's Jelly. The umbilical vein have a wider lumen and a thinner wall than the umbilical arteries. (Jane. A Bates, 2004).

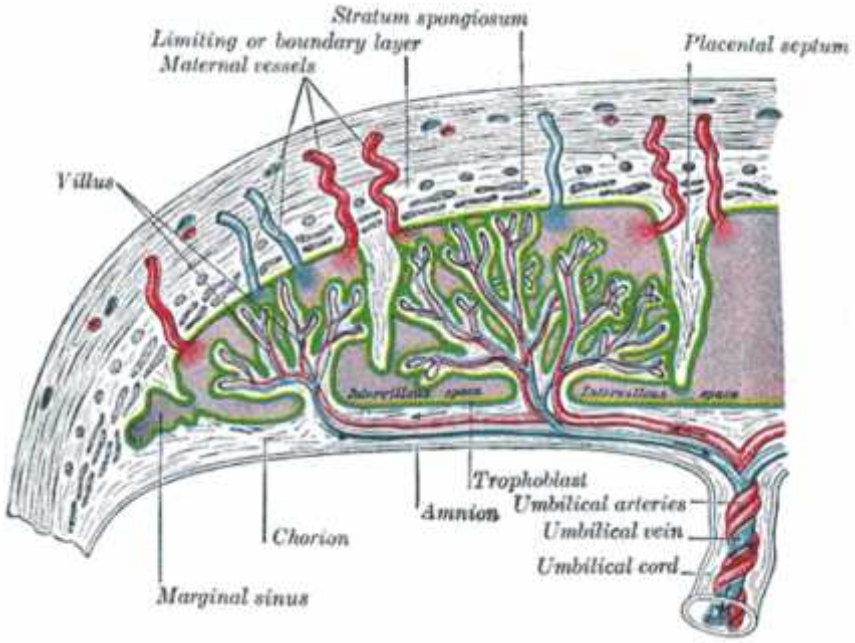


Figure: The connection of umbilical artery (UA) with placenta (Chudleigh et al 2004)

Connection of umbilical cord to foetal circulatory system:

The umbilical cord enters the fetus via the abdomen, at the point which after separation become the umbilicus. Within the fetus, the umbilical vein runs towards the transverse fissure of the liver, where it divides into two branches. One of these branches joins with the hepatic portal vein which carries blood into the liver. The second branch known as the ductus venosus allows the majority of the incoming blood (almost 80%) to bypass the liver and flow via the left hepatic vein into the inferior vena cava, which c**a**rries blood towards the heart. The two umbilical arteries branch from the internal iliac arteries, and pass on either side of the urinary bladder.(Jane. A Bates, 2004)

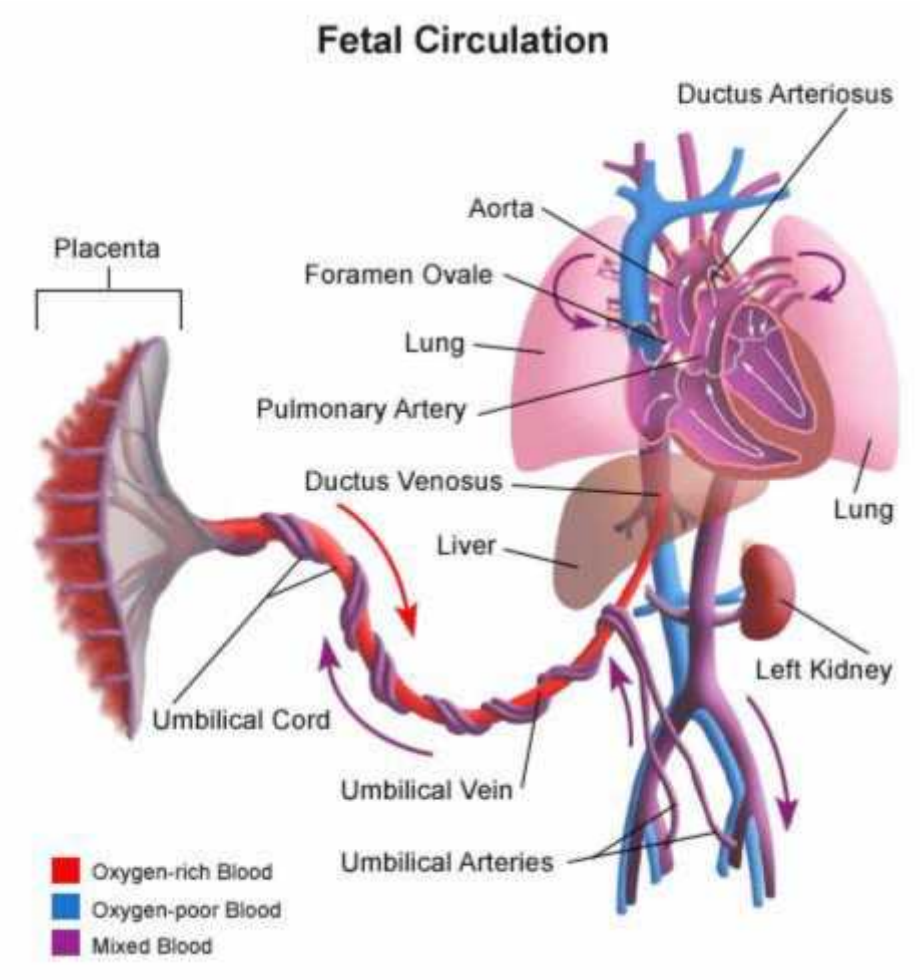


Figure: The foetal circulation

Within the child, the umbilical vein and ductus venosus seal, and degenerate into fibrous remnants called as round ligament of the liver and the ligamentum venosum respectively. Part of each umbilical artery seal and degenerating into medial umbilical ligaments, while the remaining sections are retained as part of the circulatory system. After birth, the umbilical cord is clamped or tied and is then cut. The stump of the cord that remains attached to the baby wilts away and falls off after few days, leaving the circular depression in the abdomen known as the umblicus. (Jane. A Bates, 2004).

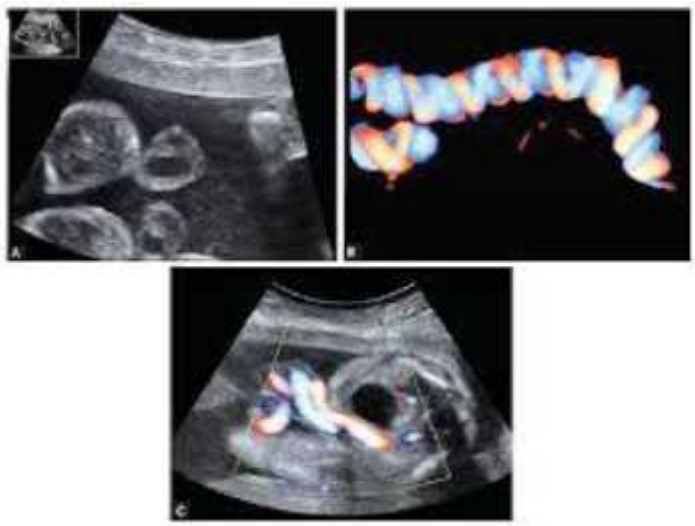


Figure : Umbilical artery in ultrasound image

Anatomy of middle cerebral artery (MCA):

The brain is mainly supplied by four vessels—the right and left internal carotid and vertebral arteries and receives 15% of the cardiac output. The extracranial cerebral arteries refer to all the arteries that carry blood from the heart up to the base of the skull. The left and right sides of the extracranial circulation are asymmetrical. On the left side, the common carotid (CCA) and subclavian arteries arise directly from the aortic arch, whereas on the right side the brachiocephalic artery, also known as the innominate artery, arises from the aorta and divides into the subclavian artery and CCA. The CCA, which has no branches, divides into the internal and external carotid arteries, but the level of the carotid bifurcation in the neck is highly variable. (Edoardo et al, 2007).

In approximately 90% of cases, the internal carotid artery (ICA) lies posterolateral or lateral to the external carotid artery (ECA) and, unlike the ECA, has no branches below the skull. The proximal branches of the ECA are the

superior thyroid, lingual, facial and maxillary arteries. The carotid artery widens, at the level of the bifurcation, to form the carotid bulb. In some cases, the carotid bulb may only involve the proximal ICA, and not the distal CCA, and the degree of widening of the carotid bulb is quite variable. Within the skull, the distal segment of the ICA follows a curved path, known as the carotid siphon. The most important branch of the ICA is the ophthalmic artery, which supplies the eye. The terminal branches of the ophthalmic artery, the supratrochlear and supraorbital arteries, unite with the terminal branches of the ECA. (Edoardo et al, 2007).The ICA finally divides into the middle cerebral artery (MCA) and the anterior cerebral artery (ACA). The posterior circulation of the brain is mainly supplied by the left and right vertebral arteries, via the basilar artery. The vertebral artery is the first branch of the subclavian artery, 21 arising from the highest point of the subclavian arch.

THE DOPPLER ULTRASOUND

Doppler ultrasound offers a non-invasive method for analysis of fetal hemodynamics. Study of the uterine and umbilical arteries gives data on the perfusion of the uteroplacental and fetoplacental circulations, respectively, while Doppler studies of selected fetal organs are valuable in detecting the hemodynamic rearrangements that occur in response to fetal hypoxemia.

Direct readings of the uterine artery flow was also gained by means of electromagnetic techniques. Only the incorporation of the Doppler effect to the ultrasound equipment by Stromura, has enabled Fitzgerald and Drumm, for the

first time to study the maternal-fetal circulation in a non-invasive and physiological way.

Principle of Doppler:

The Doppler Effect is defined as the observed changes in the frequency of transmitted waves when relative motion exists between the source of the wave and the observer. The frequency increases when the source and the observer move closer and decreases when they move apart.The phenomenon bears the name of its discoverer, Christian Andreas Doppler, an Austrian mathematician and physicist in 1842.

The change in frequency of the energy wave transmission is known as the Doppler frequency shift or simply the Doppler shift.The Doppler effect is observed irrespective of whether the observer or the source moves.[87]

Doppler Velocimetry

1) Qualitative assessment: Achieved visually by evaluating the waveform or the colour distribution. Blood flow can also be qualitatively assessed by listening to Doppler signals.

2) Quantitative assessment: Allows measurement of velocity. Doppler measurements can be considered reliable as long as the insonant angle is 60 degrees. Velocity measurements most commonly in pulsed Doppler are maximum peak systolic velocity, highest time averaged maximum velocity and minimum diastolic velocity.

3) Semi-quantitative assessments:

The relationship between systolic and diastolic components of waveform is evaluated and angle dependence which is important in quantitative measurements becomes less important.

Commonly used indices available on most commercial scanners are: [88]

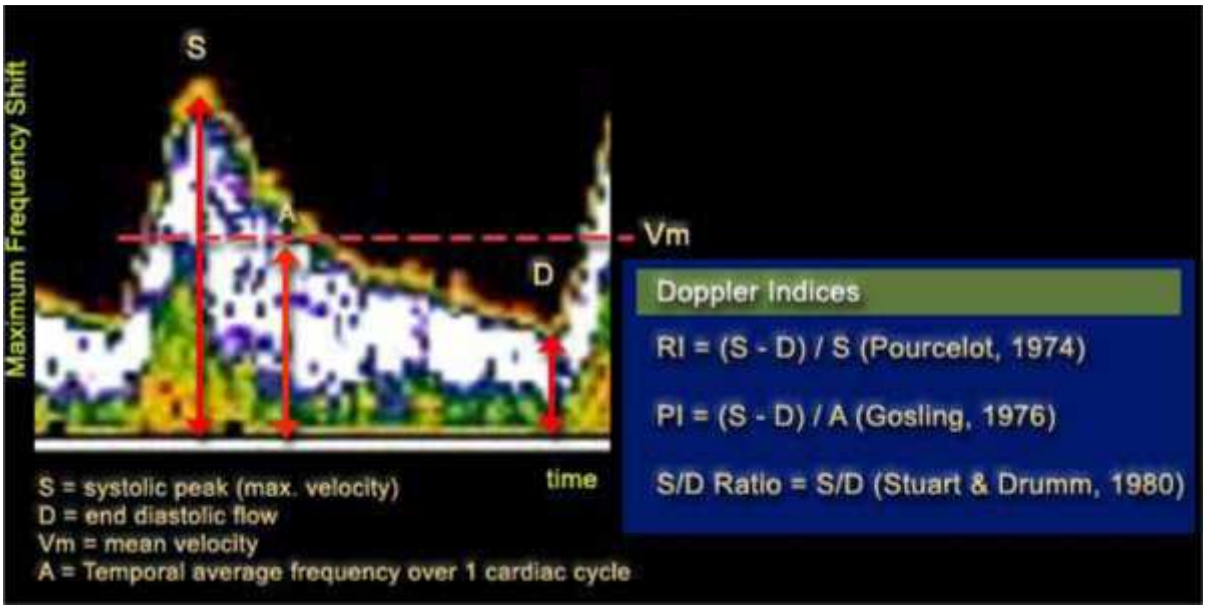
(1) Resistance index (RI)

(Also called resistive index or Pourcelot's index) =(S-D)/S

(2) Systolic/diastolic (S/D) ratio, sometimes called the A/B ratio

(3)Pulsatility index (PI) = (S-D)/A

Figure: Doppler indices



These indices are all based on the maximum Doppler shift waveform.The PI takes slightly longer to calculate than the RI or S/D ratio because of the need to measure the mean height of the waveform.

PI is a better index in obstetric Doppler because,

- When diastolic velocity=0, RI will always be 1, while PI could be any value more than 1.So PI is more informative in such situations
- PI takes the entire waveform into account and not just the maximum and minimum frequencies as in RI.

Doppler study of Utero-placental circulation

With Doppler as a screening test, several studies have proved a significant relationship between flow velocity waveform of uterine arteries with the subsequent development of pre-eclampsia, IUGR, placental abruption and preterm delivery.

The morphologic changes happening in the uterine vasculature can be established by the colour and pulsed Doppler with detection and analysis of main uterine arteries and their ramifications into arcuate and radial arteries up to their spiral artery terminal branches. The blood flow velocity increases in the uteroplacental circulation, while its impedance decreases as gestation advances.

Umbilical artery Doppler

Doppler velocimetry of the umbilical artery evaluates the resistance to blood perfusion of the feto-placental unit. Maternal or placental circumstances that

obliterate small muscular arteries in the placental tertiary stem villi ends up in a gradual reduction in end-diastolic flow in the umbilical artery. Reversed end-diastolic flow in the umbilical arterial circulation indicates an upgraded stage of placental compromise and they are related to obliteration of 70% of artery.9,10 It is frequently with severe IUGR with foetal weight up to less than 3rd percentile and smotimes oligohydramnios.11,12 The S/D ratio and pulsatility index (PI) are regularly used and they are sufficient to manage most cases of suspected IUGR. When end-diastolic flow is absent, the S/D ratio is immeasurable and PI may be used.

Middle cerebral artery Doppler

The middle cerebral arteries, which contributes to 80% of the cerebral circulation, represent major branches of the circle of Willis and are the most accessible cerebral vessels for ultrasound imaging in the fetus. 15. Very minimal studies have proved that middle cerebral artery peak systolic velocity may be a better predictor of perinatal mortality in preterm IUGR than the PI, but additional study is needed to confirm this finding.17 When there is fetal hypoxemia, there will be brain-sparing reflex, which is specified by increased end-diastolic flow velocity which is indicated by a low PI in the middle cerebral artery14, 18, 19

Ductus venosus Doppler

Ductus venosus Doppler waveforms are biphasic with the first peak corresponding to ventricular systole, the second peak during passive filling in ventricular diastole, followed by a nadir in late diastole with atrial contraction. Decreased, absent, or reversed flow in the A wave during atrial contraction may

represent myocardial impairment and increased ventricular end-diastolic pressure resulting from an increase in right ventricular afterload. This abnormal waveform in the ductus venosus has been recognised in foetuses with IUGR and related to an augmented neonatal mortality rate.23,24

Uterine artery Doppler

Doppler velocimetry of the uterine arteries discloses a progressive reduction in impedance with progressing gestational age.25,26 This decrease in impedance is thought to reflect a maternal adaptation to pregnancy resulting from trophoblastic invasion of the maternal spiral arterioles in the first half of gestation.27 In early trimester , a notched uterine artery Doppler waveform and low diastolic flow is obvious due to high vascular impedance. With advancing gestation, decreasing vascular impedance is reflected by increased flow in diastole and in disappearance of the notch. The persistence of a uterine artery notch in the late second and third trimesters is indicative of some abnormality.23,29,30 Also if the PI, with a value of more than 95th percentile for gestational age taken as abnormal31

TABLE

Characteristics of common Doppler studies

Variable	Gestational age, wk	Location	Pitfalls	Abnormal	Abnormality linked with
Umbilical artery	>23	Abdominal cord insertion (preferred), other locations acceptable	Optimally done when no fetal breathing	Decreased end-diastolic flow (includes AEDF, REDF)	Stillbirth Neurological impairment
Middle cerebral artery	>23	Proximal portion of vessel at 0-degree angle of incidence	>30-degree angle of incidence	Increased diastolic flow[a]	Neonatal acidosis Neurological impairment
Ductus venosus	>23	At site of aliasing, where it branches from umbilical vein	Obtaining Doppler of inferior vena cava	Decreased, absent, or reversed flow in a wave	Neonatal acidemia Perinatal mortality
Uterine artery	18-23	As it crosses the hypogastric vessels	Obtaining Doppler of hypogastric artery or vaginal branch of uterine artery	Notching or elevated pulsatility index	Linked in some studies with prediction of IUGR

AEDF, absent end-diastolic flow; IUGR, intrauterine growth restriction; REDF, reversed end-diastolic flow.

[a] May use gestational age–based table[15] or subjective.

SMFM. Doppler assessment of fetus with IUGR. Am J Obstet Gynecol 2012.

Currently, Doppler velocimetry of utero placental, umbilical, and foetal vessels has turned up into established method for antenatal monitoring (Baschat and Gembruch, 2003, Dubiel et al., 2000).

Circulatory changes, seen in certain foetal Doppler waveforms, foresee adverse perinatal outcome (Arduini and Rizzo, 1993). Recent studies have shown the efficacy of the middle cerebral artery (MCA) Doppler assessment (Bahlmann et al., 2002).

Of the late, with the development of pulsed and color-coded Doppler combined with better reproducibility, the MCA has emerged as the vessel of choice in the Doppler assessment of fetal intracranial as well as other organs perfusion (Mari et al., 1989).Also A. S. M. et al 2004 had studied foetal heart rate and umbilical artery flow velocity variability in intrauterine growth restriction. Heart rate variability was significantly reduced in the presence of

growth restriction, but no significant difference was demonstrated for blood flow velocity variability, the LH ratio for heart rate variability was significantly reduced in the presence of growth restriction.

Applicability of Doppler indices in the diagnosis of abnormalities is possible only when there are reference normal values for each index. (Manning et al., 1980, Wellek and Merz, 1995).This study is intended to analyse the use of above indices in suspected IUGR babies and by analysing the relationship of abnormal indices and future morbidity, so that can start antepartum management for those mothers.

MATERIAL AND METHODOLOGY

Material of Study

Tools and equipment:

The Umbilical (UA), Ductus venosus (DV), uterine artery and Middle cerebral (MCA) arteries Doppler should be executed only with suitable instrumentation. The current standard of practice in this research includes the tools and equipment which used efficiently and precisely to give the desired expected results planed previously in the hypothesis

Ultrasound system:

The applied ultrasound unit was a General Electric (GE) medical system, logic 5 expert

Ultrasound Transducer: The applied ultrasound Transducer was a convex probe with a frequency of 3.5MHz

Patient preparation:

The Doppler ultrasound of umbilical, middle cerebral arteries and ductus venosus in Intra Uterine Growth Restriction (IUGR) has been scanned without previous preparation; only short orientation and aware of the nature of the study and had to willingly, provide informed consent before entering the study.

Method of the study:

Sample selection:

This study has been carried out in Tirunelveli medical college, Department of Obstetrics & Gynaecology.

The population of study is pregnant women attending OG OPD with high risk pregnancy and diagnosed as suspected intrauterine growth restriction based on *symphysis fundal height if less than 10th percentile.* All patients were first scanned at 20-22 weeks

Exclusion criteria:

1. Pregnant mother with normal SFH
2. Congenital malformation and chromosomal abnormalities,
3. Twin's pregnancy and
4. Oligohydramnios

The sample size was 50 pregnant women with high risk for IUGR at 3rd trimester

Patient position:

The mother undergoing study is scanned to visualize the umbilical and middle cerebral arteries in the supine position with knee support with head of bed elevated 30 degree, and a coupling medium (e.g., gel) is applied to the transducer to reduce the interference that may be introduced by air between the transducer and the skin.

The umbilical arteries will be studied by identifying within the amniotic fluid by the presence of parallel line echoes, which displayed a pulsatile activity on real time image, the Power Doppler (PD) followed by Pulse Wave Doppler

(PWD) modes were applied for the spectral analysis and determination the values of peak systolic velocity (PSV) in cm/sec, end diastolic velocity (EDV) in cm/sec, resistive index (RI) and pulsatility index (PI) for each artery respectively.

The flow velocity waveforms obtained from umbilical and MC arteries will computed automatically, the program identified individual cardiac cycles and computed peak systolic velocity. End diastolic velocity and S/D ratio.

The middle cerebral artery is the most studied cerebral artery because it is easy to sample and it can be sampled at an angle of 0° between the ultrasound beam and the direction of the blood flow. Therefore, for the middle cerebral artery we are able to determine angle-independent indices (the most used is the pulsatility index) and also the real velocity of blood flow

So we analysed by taking into account of following parameters

- Umbilical artery – decreased or absent or reversed end diastolic flow as abnormal
- Middle Cerebral Artery – Pulsatility index <1.7 taken as abnormal
- Ductus Venosus - decreased or absent or reversed waveform as abnormal
- Uterine Artery – Presence of Diastolic notch and Pulsatility index > 1.45 as abnormal.

We analysed the above parameters observed in Doppler scan done at 20 to 22 weeks and correlated with maternal and fetal outcome particularly IUGR at later stages of pregnancy and neonatal period

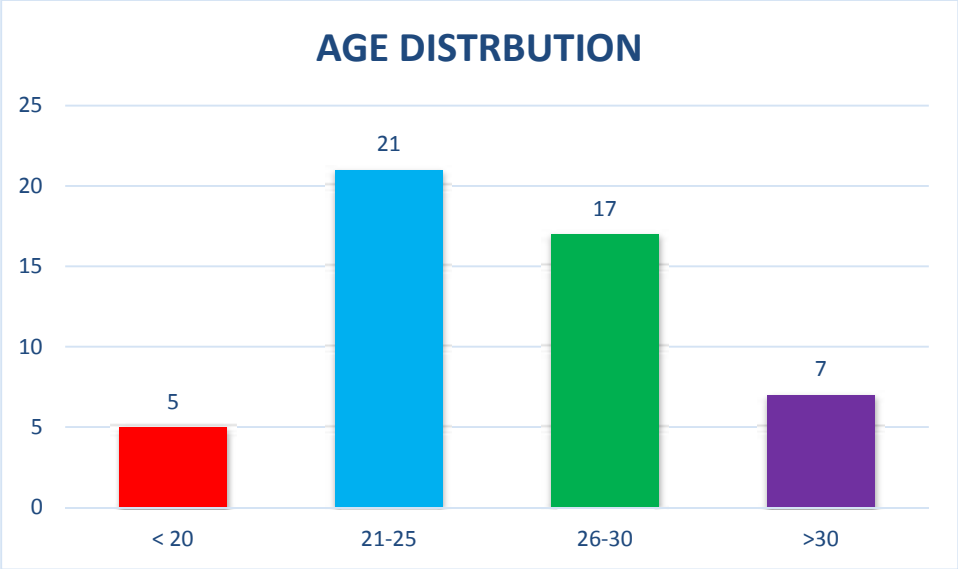
Data analysis:

The collected data entered in a master sheet and enter the computer and analysed by IBM SPSS Version 21.0 and frequency tables and presented in form of graphs, table and figures.

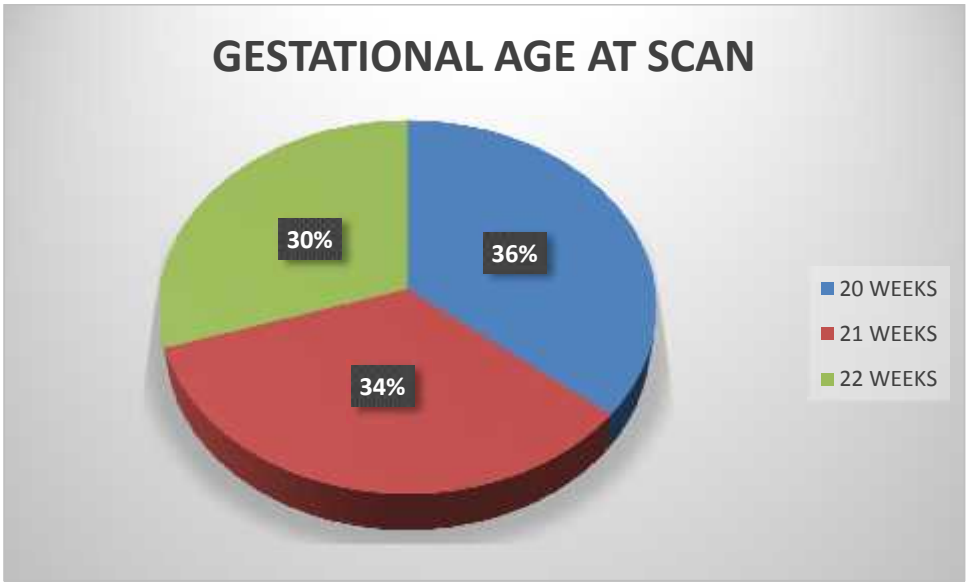
OBSERVATION & RESULTS

AGE DISTRIBUTION

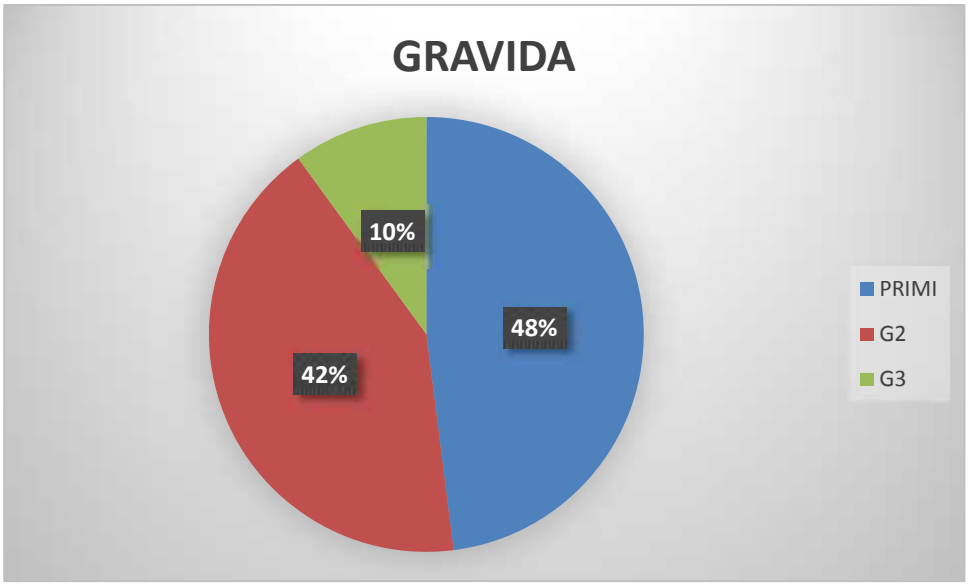
AGE (IN YEARS)	NO OF PATIENTS	PERCENTAGE
< 20	5	10%
21-25	21	42%
26-30	17	34%
>30	7	14%



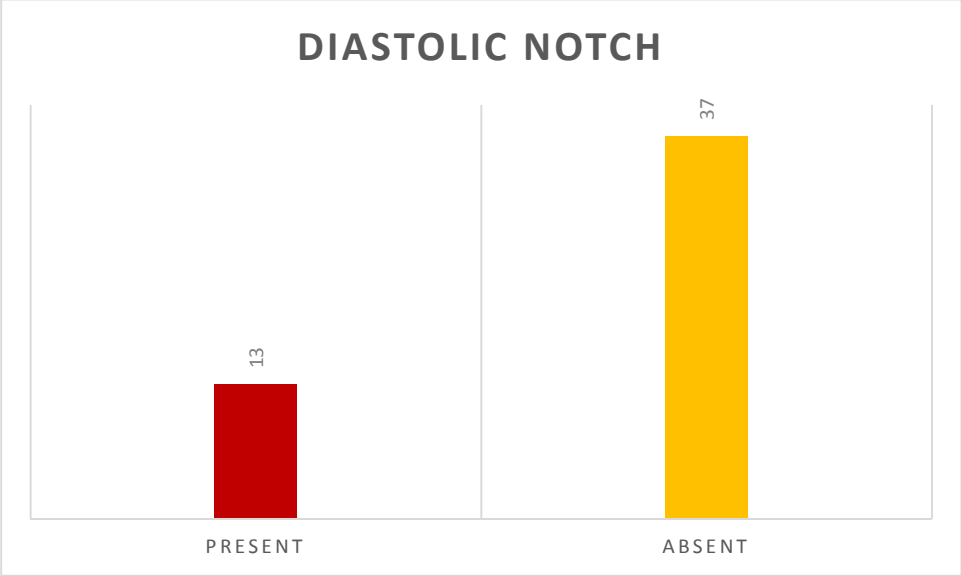
GESTATIONAL AGE @ SCAN	NO OF PATIENTS	PERCENTAGE
20 WEEKS	18	36%
21 WEEKS	17	34%
22 WEEKS	15	30%



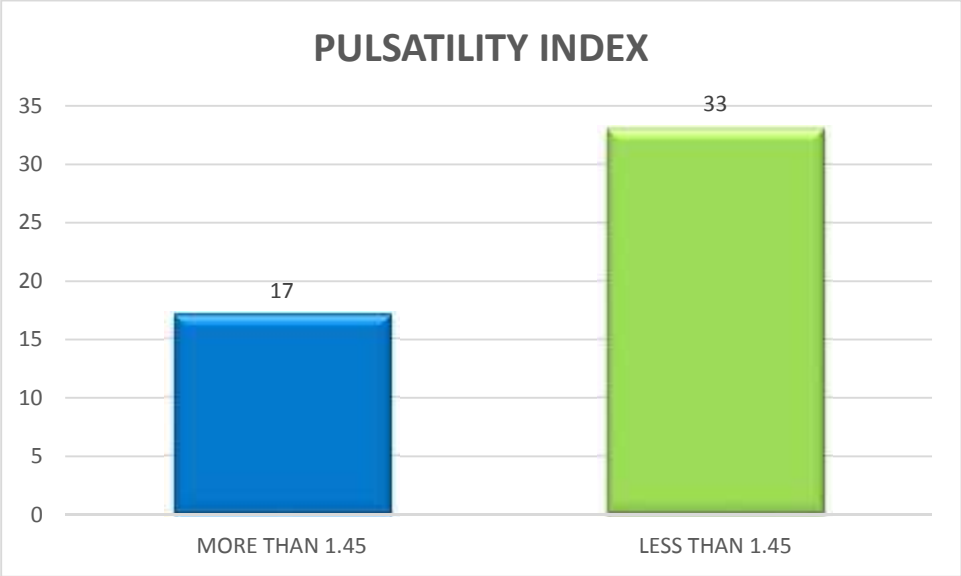
GRAVIDA	NO OF PATIENTS	PERCENTAGE
PRIMI	24	48%
G2	21	42%
G3	5	10%



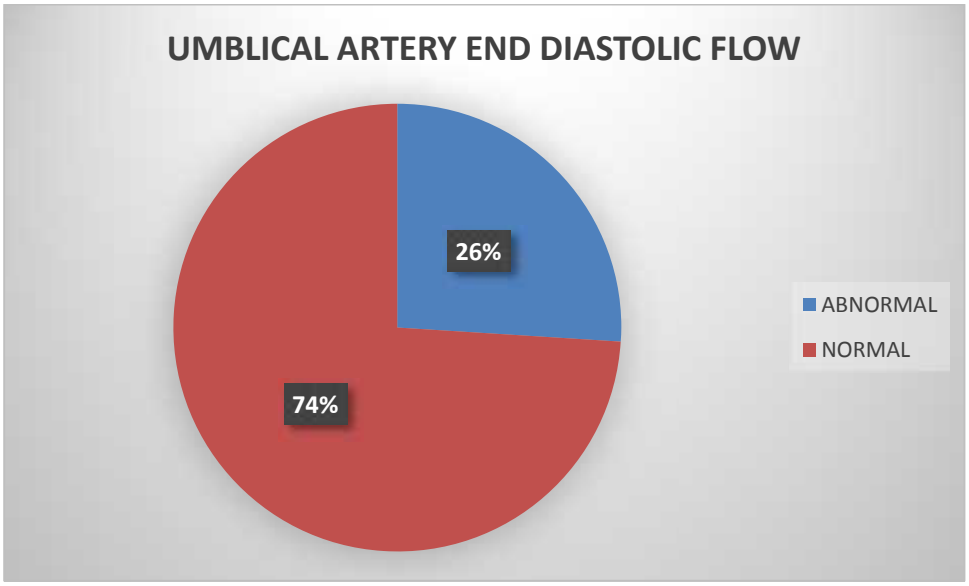
DIASTOLIC NOTCH	NO OF PATIENTS	PERCENTAGE
PRESENT	13	26%
ABSENT	37	74%



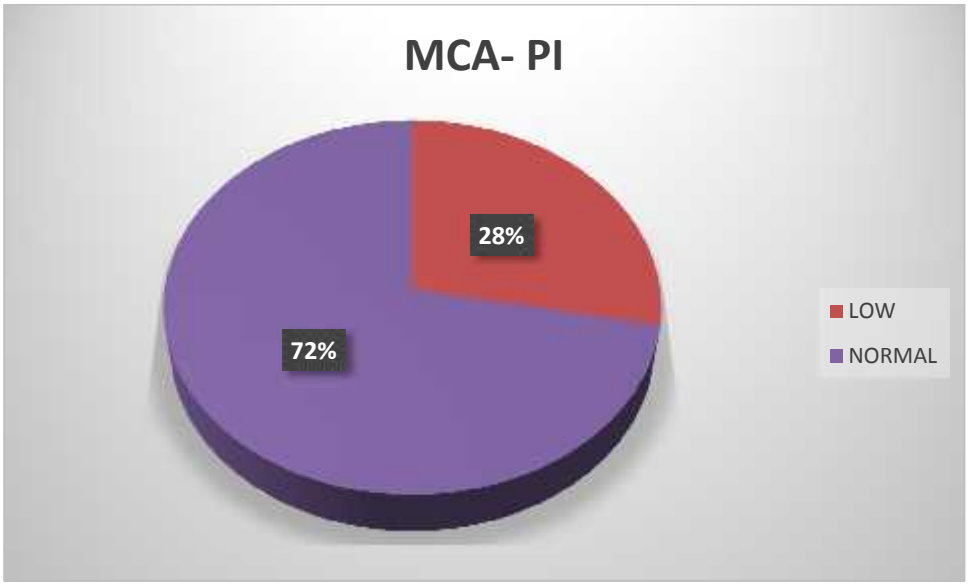
PULSATILITY INDEX	NO OF PATIENTS	PERCENTAGE
MORE THAN 1.45	17	34%
LESS THAN 1.45	33	66%



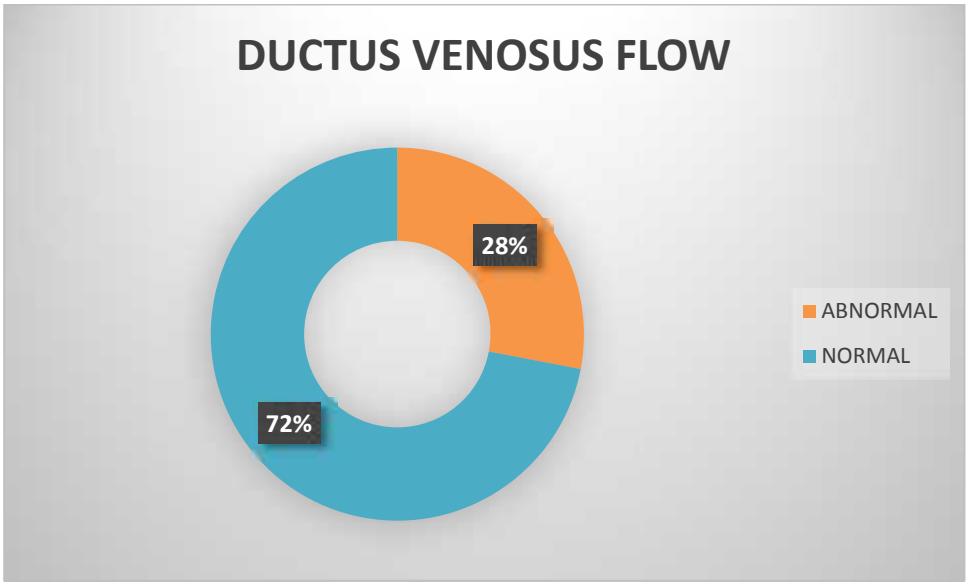
UMBLICAL ARTERY EDF	NO OF PATIENTS	PERCENTAGE
ABNORMAL	13	26%
NORMAL	37	74%



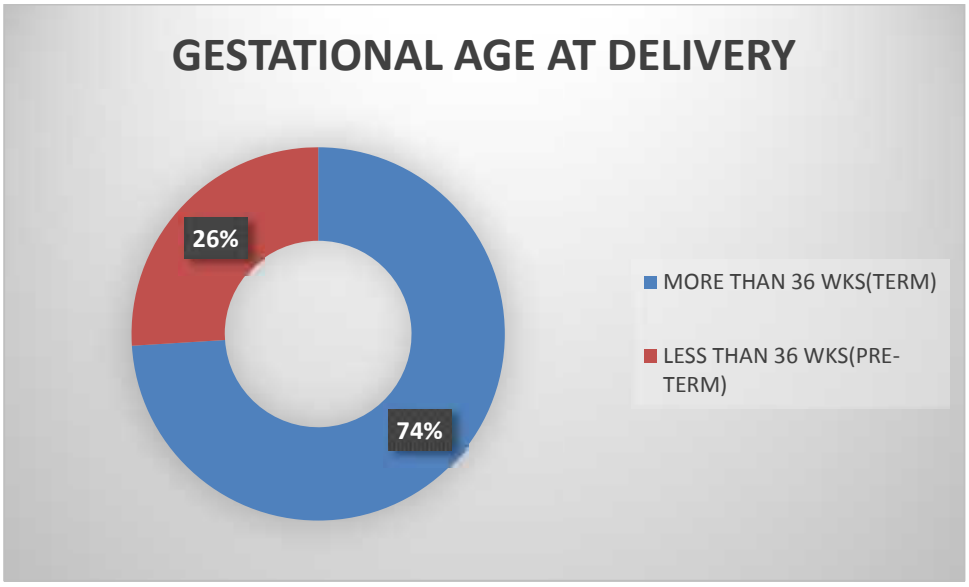
MCA - PI	NO OF PATIENTS	PERCENTAGE
LOW	14	28%
NORMAL	36	72%



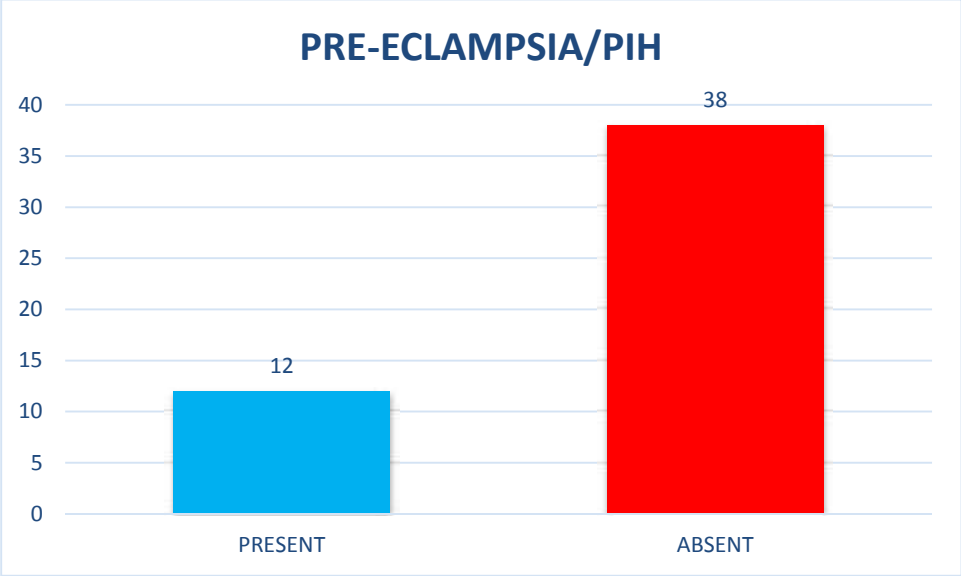
DUCTUS VENOSUS FLOW	NO OF PATIENTS	PERCENTAGE
ABNORMAL	14	28%
NORMAL	36	72%



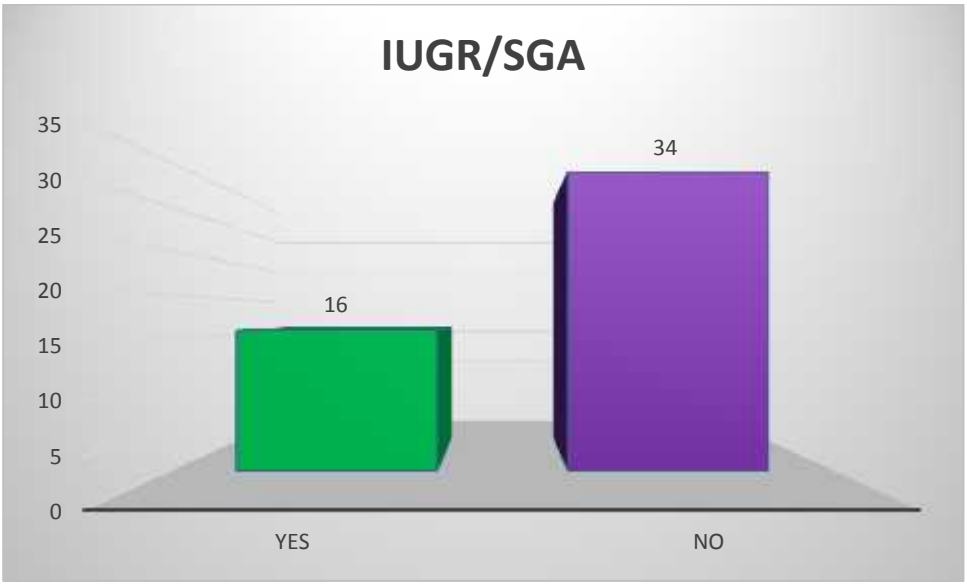
GA AT DELIVERY	NO OF PATIENTS	PERCENTAGE
MORE THAN 36 WKS(TERM)	37	74%
LESS THAN 36 WKS(PRE-TERM)	13	26%



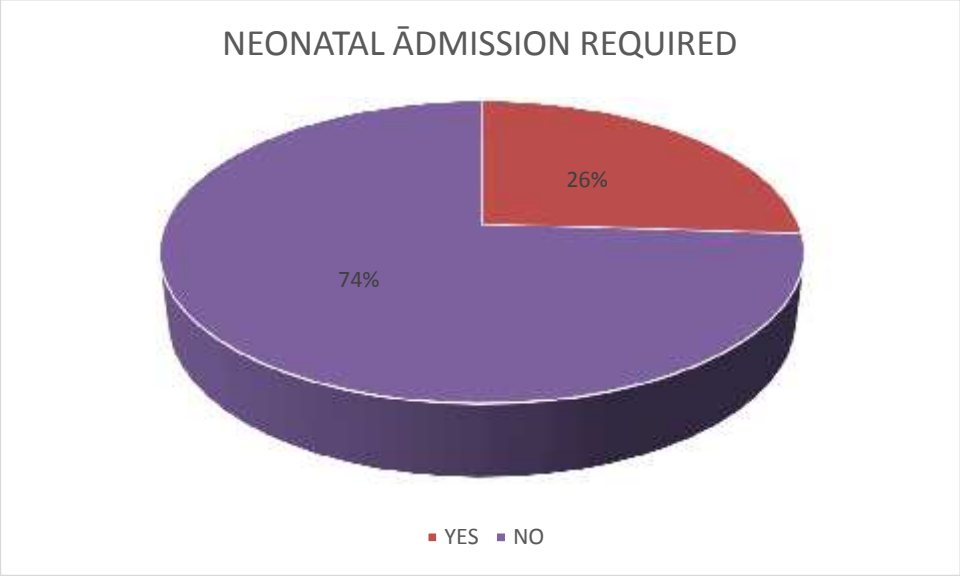
PREECLAMPSIA/PIH	NO OF PATIENTS	PERCENTAGE
PRESENT	12	24%
ABSENT	38	76%



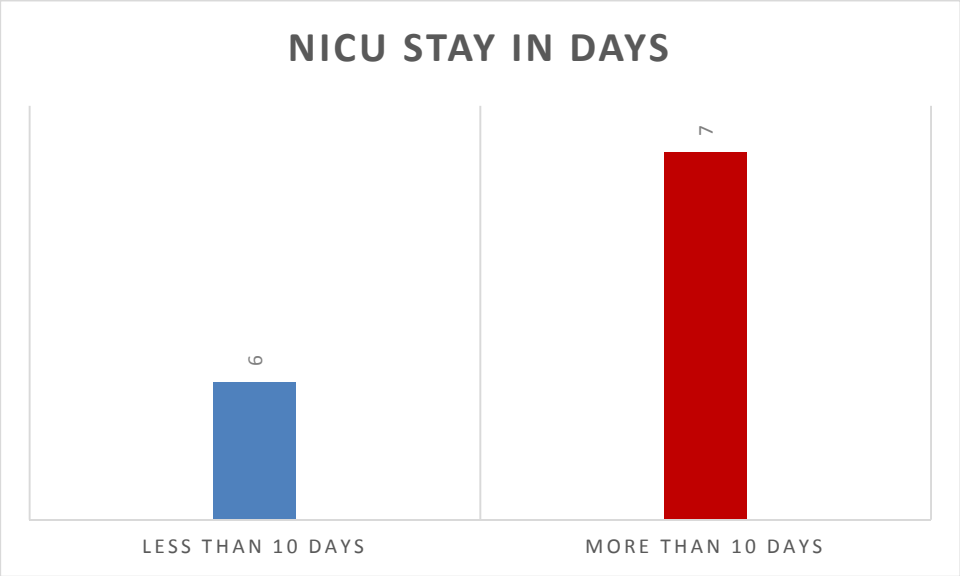
IUGR/SGA	NO OF PATIENTS	PERCENTAGE
YES	16	32%
NO	34	68%



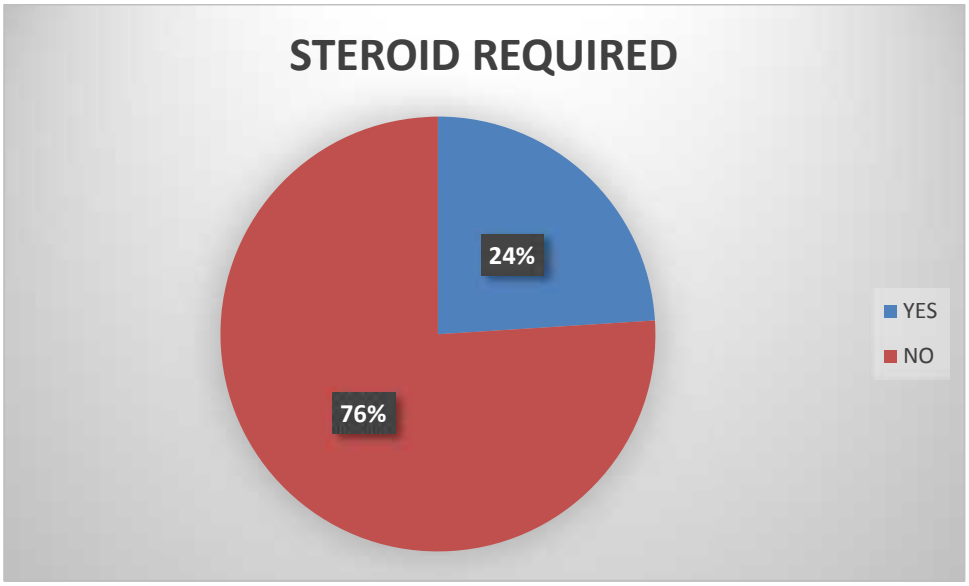
NICU ADMISSION REQUIRED	NO OF PATIENTS	PERCENTAGE
YES	13	26%
NO	37	74%



NO OF DAYS ADMISSION (N =13)	NO OF PATIENTS	PERCENTAGE
LESS THAN 10 DAYS	6	46%
MORE THAN 10 DAYS	7	54%

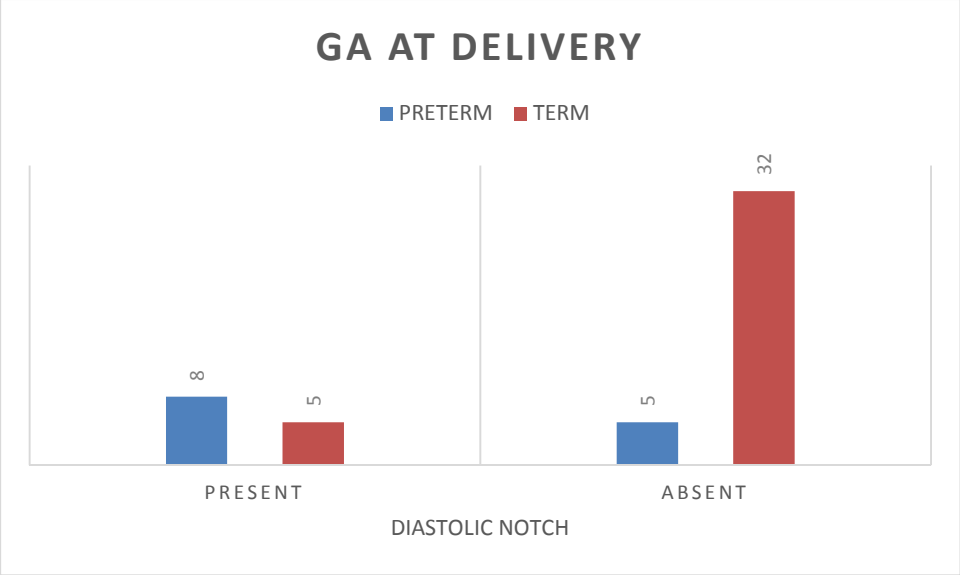


STEROID REQUIRED	NO OF PATIENTS	PERCENTAGE
YES	12	24%
NO	38	76%



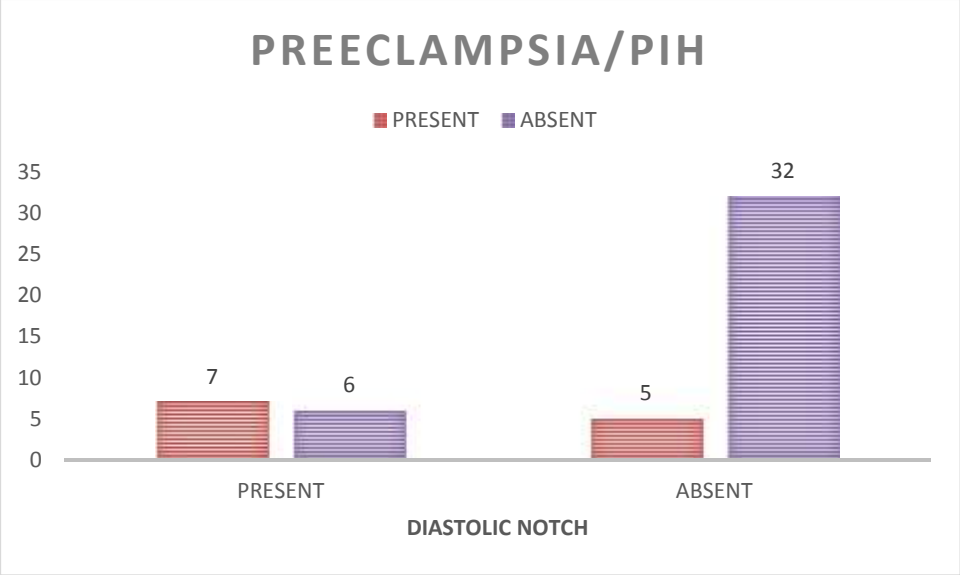
	DIASTOLIC NOTCH	
GA AT DELIVERY	PRESENT	ABSENT
PRETERM	8	5
TERM	5	32
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO- 10.24		
CHI SQUARE TEST		

Presence of diastolic notch end commonly ends up with preterm delivery with an odds ratio of 10.24 it has ten times more chance of ending up in preterm if diastolic notch is present during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



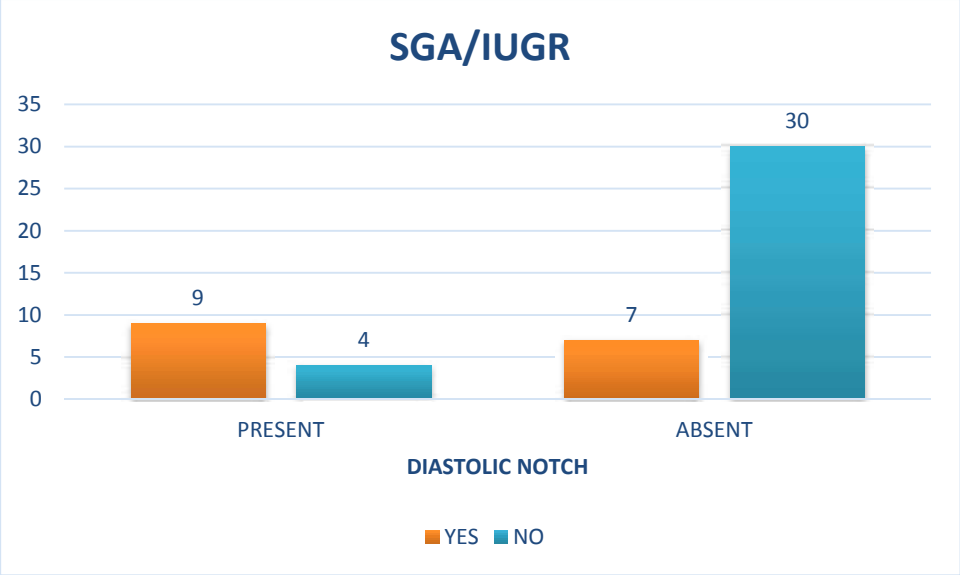
	DIASTOLIC NOTCH	
PRE ECLAMPSIA/PIH	PRESENT	ABSENT
PRESENT	7	5
ABSENT	6	32
P VALUE - 0.003		
SIGNIFICANT		
ODDS RATIO - 7.46		
CHI SQUARE TEST		

Presence of diastolic notch is related with development of pre-eclamsia or pih. With an odds ratio of 7.46 it has seven times more chance of developing PIH if diastolic notch is present during uterine Doppler at early stage. This is also statistically significant with P value of 0.003.



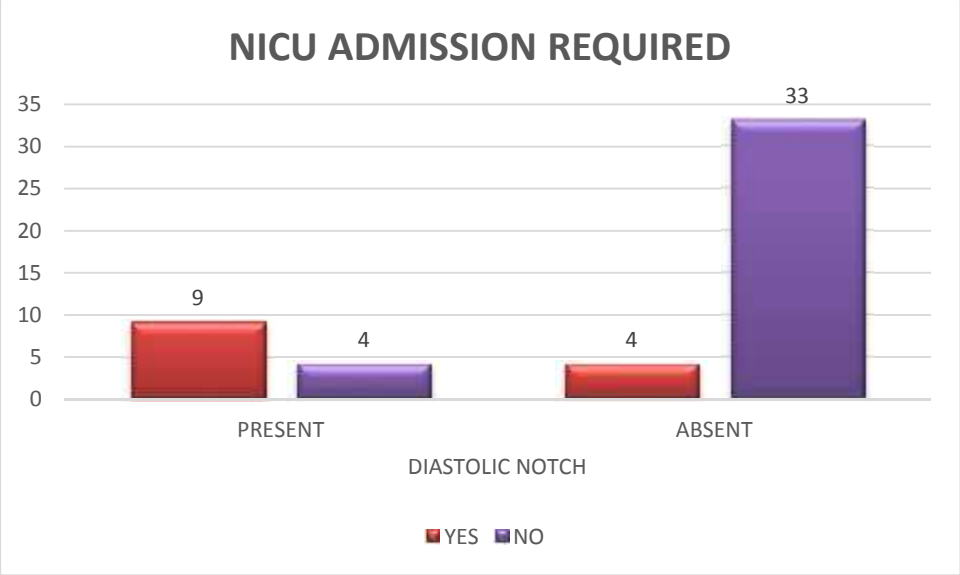
	DIASTOLIC NOTCH	
SGA/IUGR	PRESENT	ABSENT
YES	9	7
NO	4	30
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 9.64		
CHI SQUARE TEST		

Presence of diastolic notch is related with SGA/IUGR. With an odds ratio of 9.64 it has ten times more chance of developing IUGR/SGA if diastolic notch is present during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



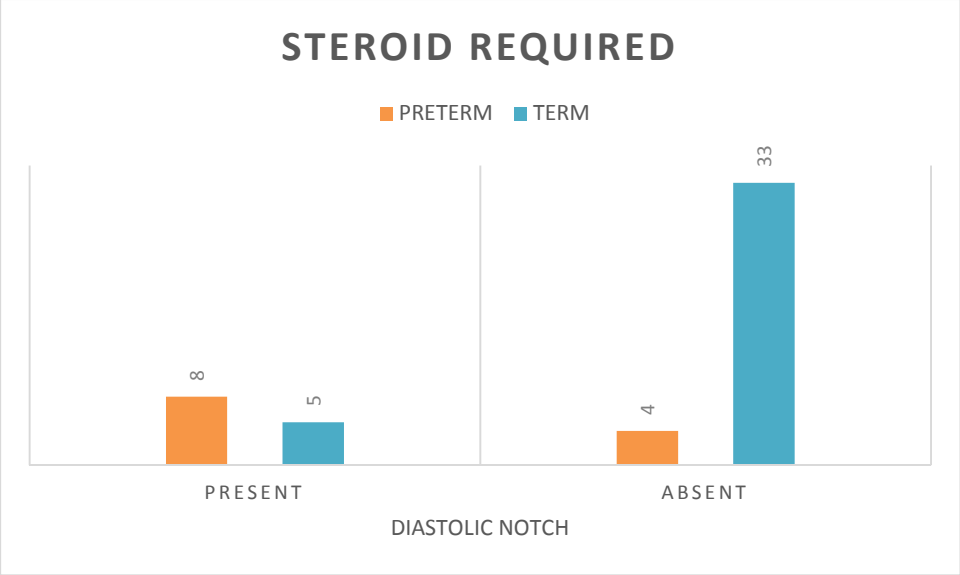
	DIASTOLIC NOTCH	
NICU ADMISSION REQUIRED	PRESENT	ABSENT
YES	9	4
NO	4	33
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 18.56		
CHI SQUARE TEST		

Presence of diastolic notch is related with admission in NICU. With an odds ratio of 18.56 it has nineteen times more chance of requiring admission in NICU if diastolic notch is present during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



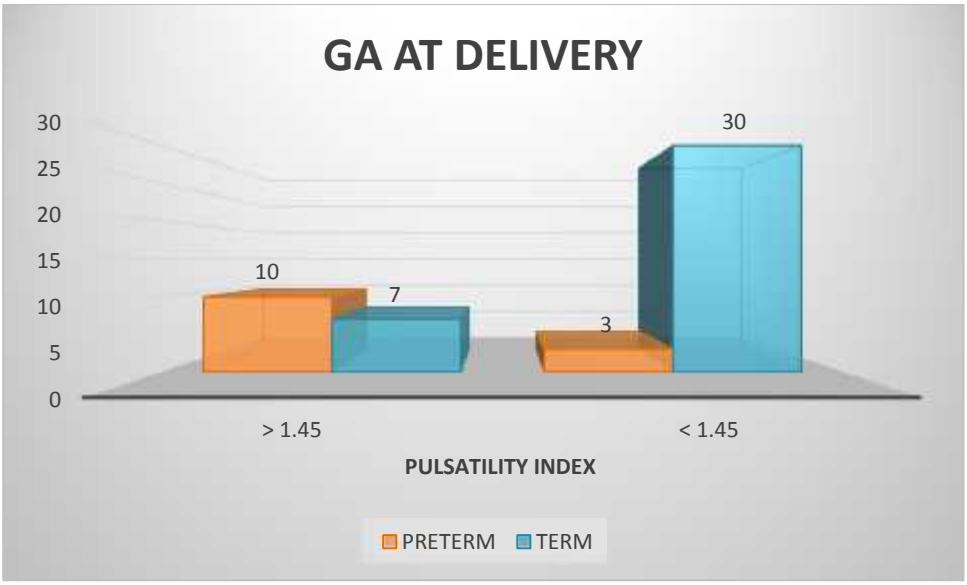
	DIASTOLIC NOTCH	
STEROID REQUIRED	PRESENT	ABSENT
PRETERM	8	4
TERM	5	33
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 13.2		
CHI SQUARE TEST		

Presence of diastolic notch is related with requirement of steroid. With an odds ratio of 13.2 it has thirteen times more chance of requiring steroids as a part of treatment if diastolic notch is present during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



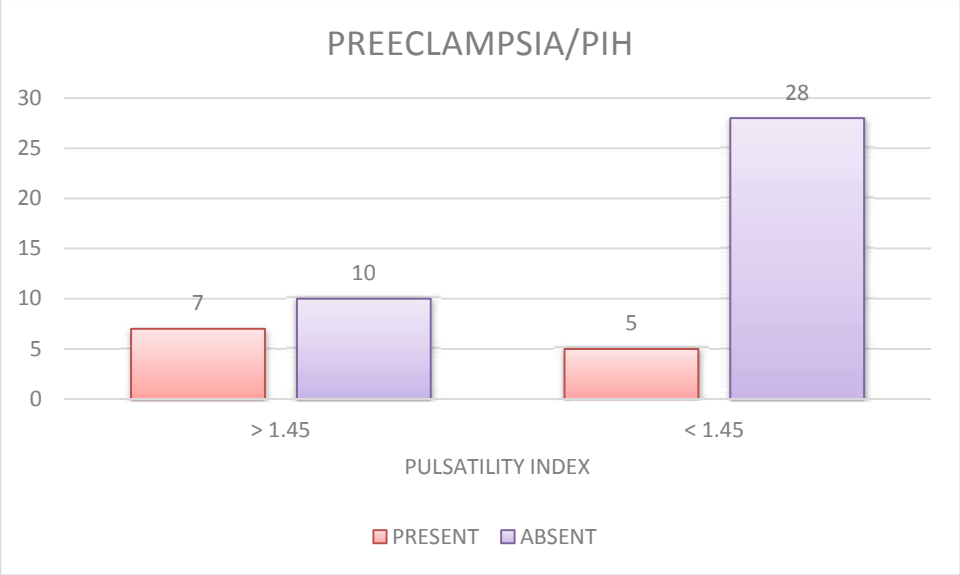
	PULSATILITY INDEX	
GA AT DELIVERY	> 1.45	< 1.45
PRETERM	10	3
TERM	7	30
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 14.28		
CHI SQUARE TEST		

Presence of high PI is related with Preterm delivery. With an odds ratio of 14.28 it has fourteen times more chance of preterm delivery if PI more than 1.45 during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



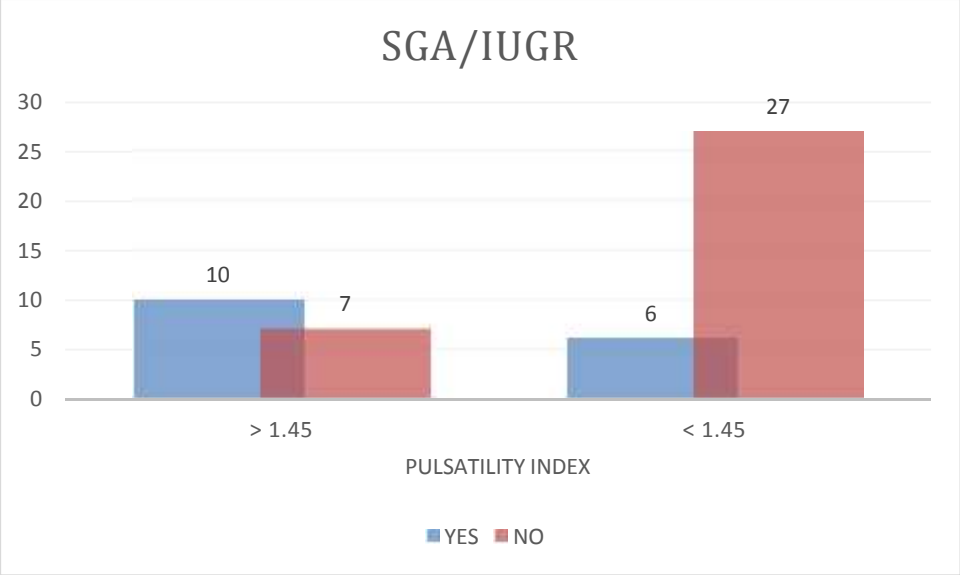
	PULSATILITY INDEX	
PRE ECLAMPSIA/PIH	> 1.45	< 1.45
PRESENT	7	5
ABSENT	10	28
P VALUE - 0.041		
SIGNIFICANT		
ODDS RATIO - 3.92		
CHI SQUARE TEST		

Presence of high PI is related with development of PIH. With an odds ratio of 3.92 it has four times more chance of PIH if PI more than 1.45 during uterine Doppler at early stage. This is also statistically significant with P value of 0.041.



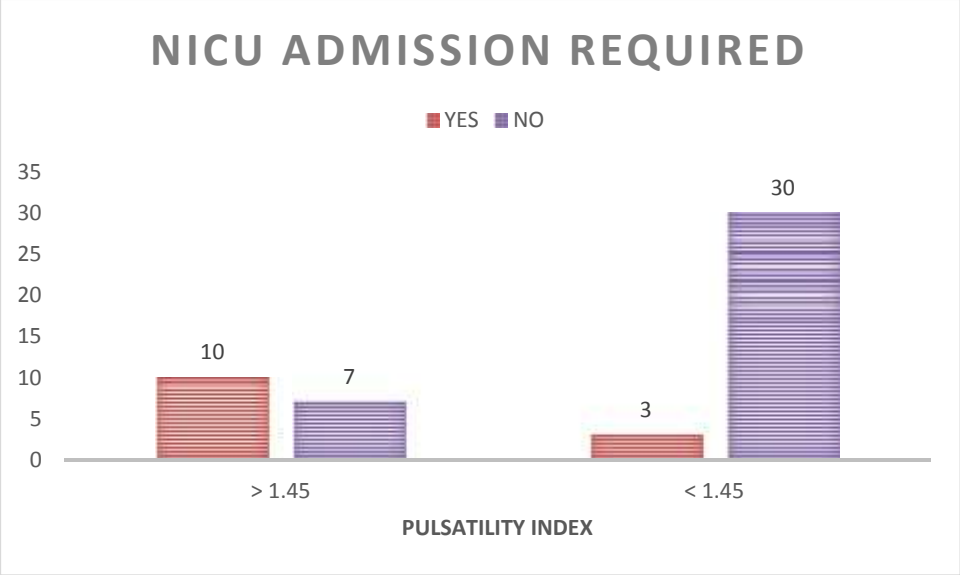
	PULSATILITY INDEX	
SGA/IUGR	> 1.45	< 1.45
YES	10	6
NO	7	27
P VALUE - 0.004		
SIGNIFICANT		
ODDS RATIO - 6.42		
CHI SQUARE TEST		

Presence of high PI is related with SGA/IUGR. With an odds ratio of 6.42 it has six times more chance of preterm SGA/IUGR if PI more than 1.45 during uterine Doppler at early stage. This is also statistically significant with P value of 0.004.



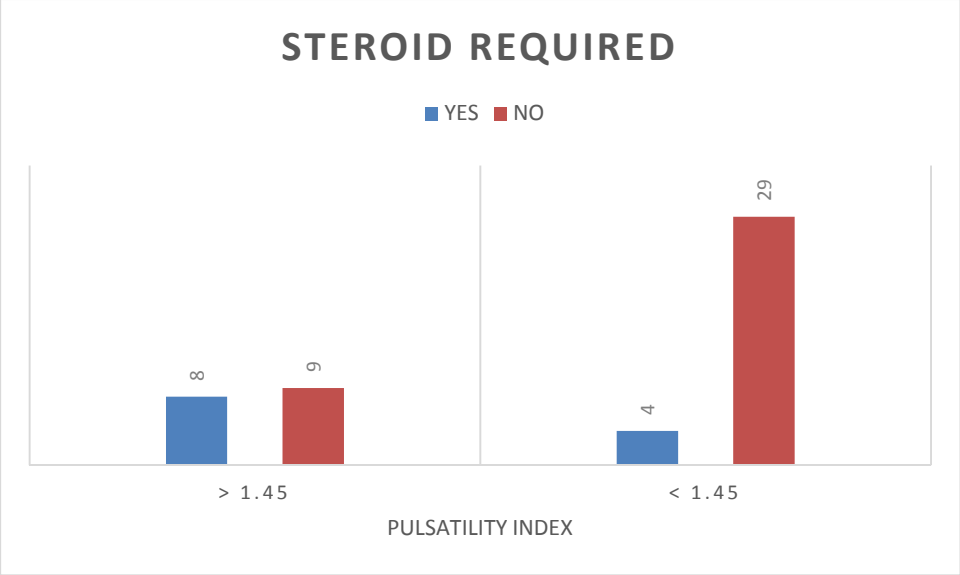
	PULSATILITY INDEX	
NICU ADMISSION REQUIRED	> 1.45	< 1.45
YES	10	3
NO	7	30
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 14.28		
CHI SQUARE TEST		

Presence of high PI is related with NICU admission. With an odds ratio of 14.28 it has fourteen times more chance of requiring admission in NICU if PI more than 1.45 during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.

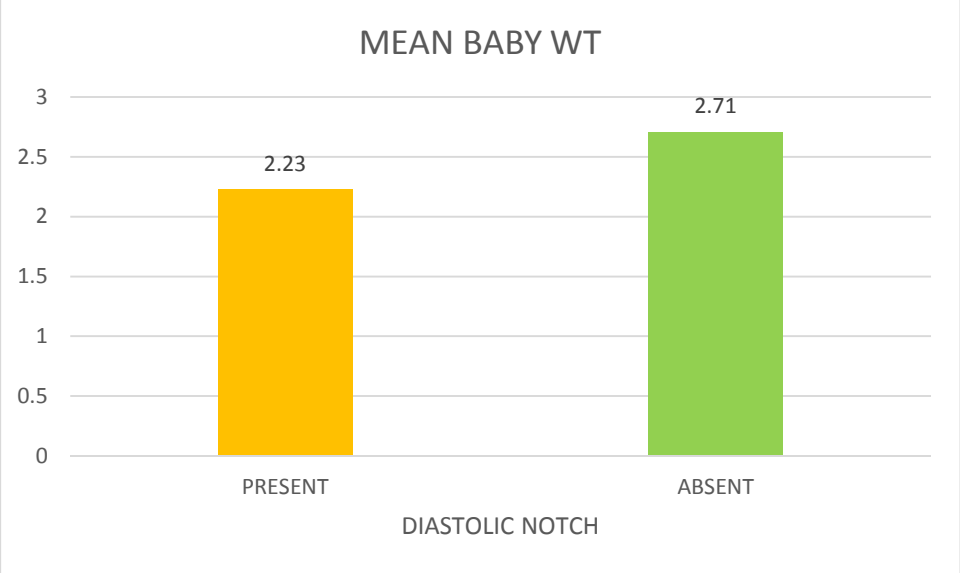


	PULSATILITY INDEX	
STEROID REQUIRED	> 1.45	< 1.45
YES	8	4
NO	9	29
P VALUE - 0.006		
SIGNIFICANT		
ODDS RATIO - 6.44		
CHI SQUARE TEST		

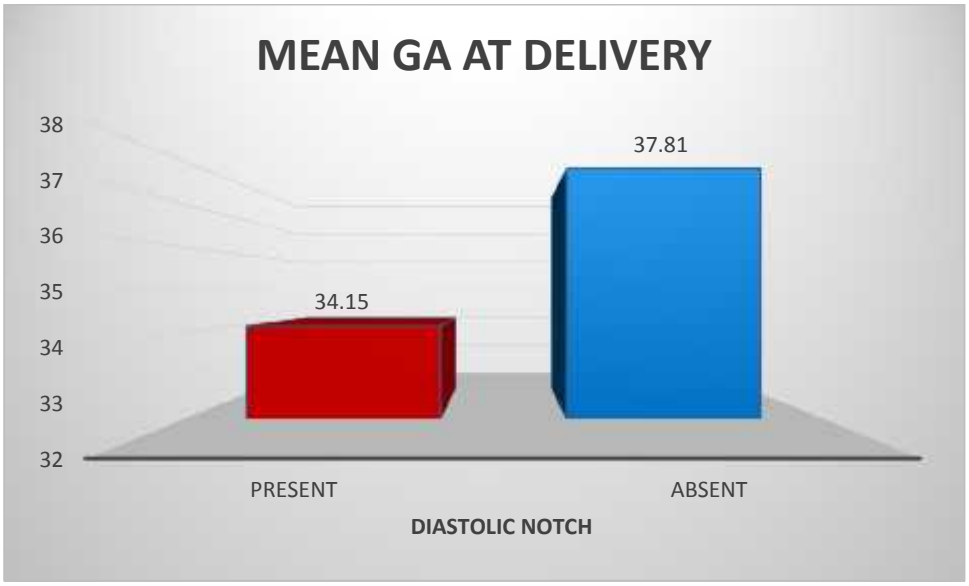
Presence of high PI is related with steroid requirement. With an odds ratio of 6.44 it has six times more chance of steroid requirement if PI more than 1.45 during uterine Doppler at early stage. This is also statistically significant with P value of 0.001.



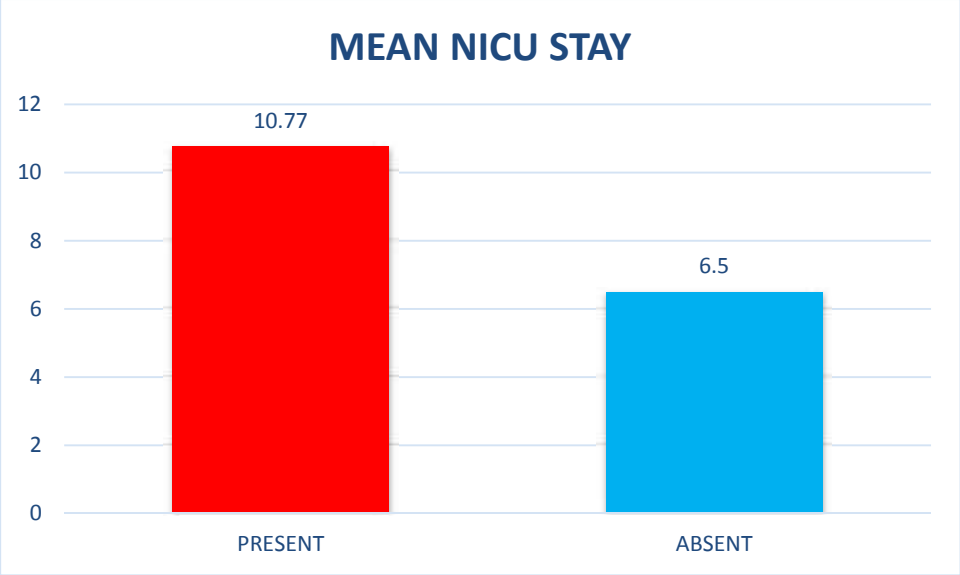
	BABY WEIGHT	
DIASTOLIC NOTCH	MEAN	SD
PRESENT	2.23	0.47
ABSENT	2.71	0.41
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		



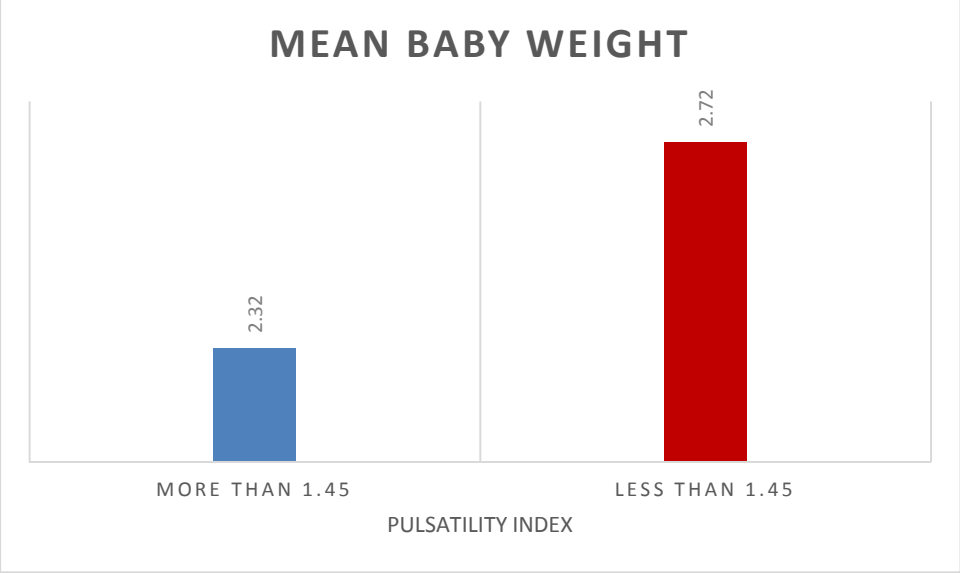
	GA AT DELIVERY	
DIASTOLIC NOTCH	MEAN	SD
PRESENT	34.15	3.1
ABSENT	37.81	2.15
P VALUE - 0.004		
SIGNIFICANT		
UNPAIRED T TEST		



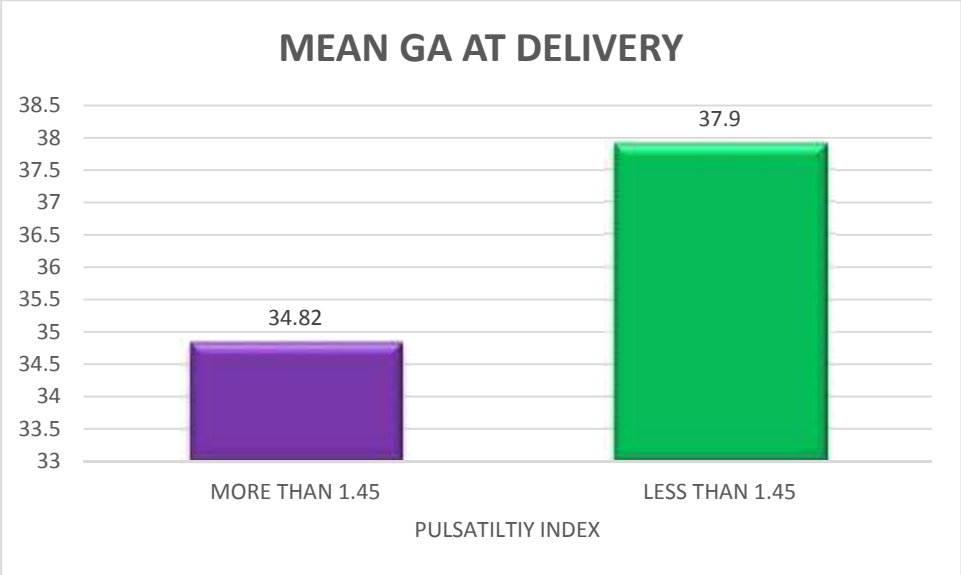
	NO OF DAYS IN NICU	
DIASTOLIC NOTCH	MEAN	SD
PRESENT	10.77	3.2
ABSENT	6.5	1.7
P VALUE - 0.042		
SIGNIFICANT		
UNPAIRED T TEST		



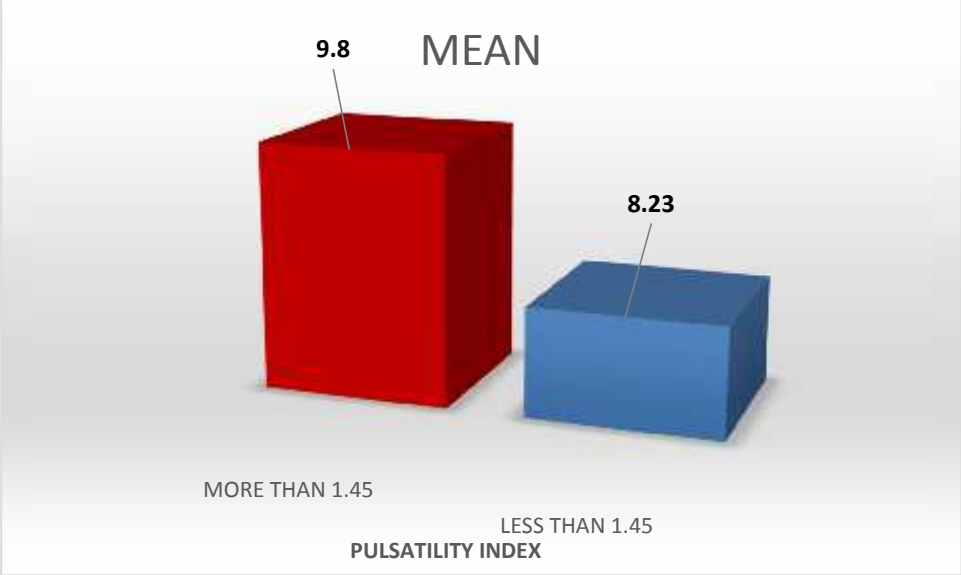
	BABY WEIGHT	
PULSATILITY INDEX	MEAN	SD
MORE THAN 1.45	2.32	0.44
LESS THAN 1.45	2.72	0.43
P VALUE - 0.004		
SIGNIFICANT		
UNPAIRED T TEST		



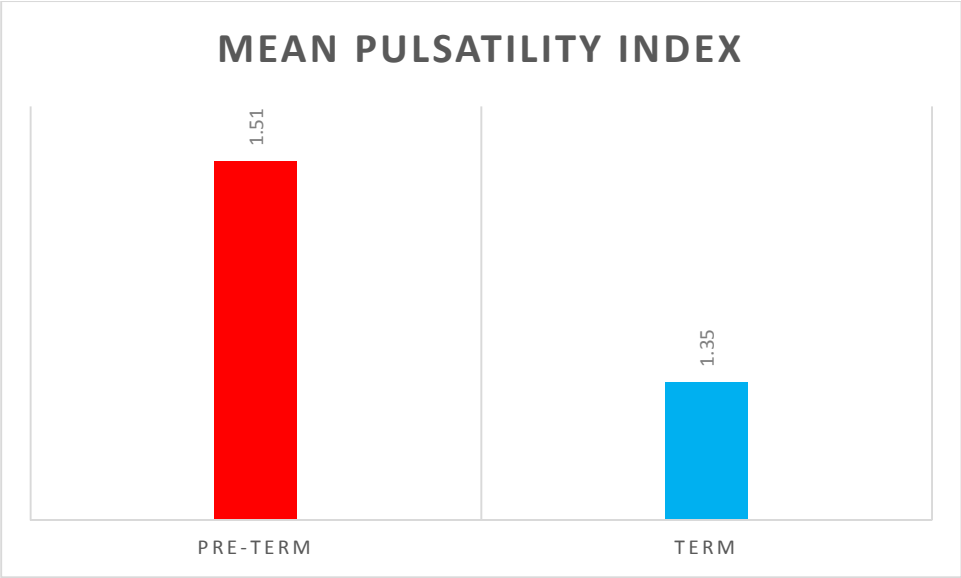
	GA AT DELIVERY	
PULSATILITY INDEX	MEAN	SD
MORE THAN 1.45	34.82	3.2
LESS THAN 1.45	37.9	2.09
P VALUE - 0.002		
SIGNIFICANT		
UNPAIRED T TEST		



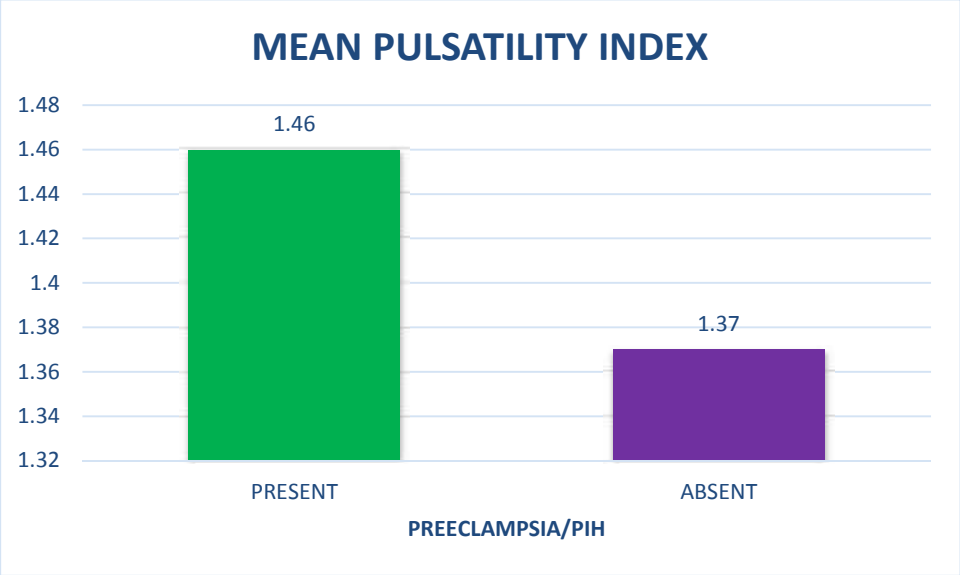
	NO OF DAYS IN NICU	
PULSATILITY INDEX	MEAN	SD
MORE THAN 1.45	9.8	2.7
LESS THAN 1.45	8.23	1.2
P VALUE - 0.021		
SIGNIFICANT		
UNPAIRED T TEST		



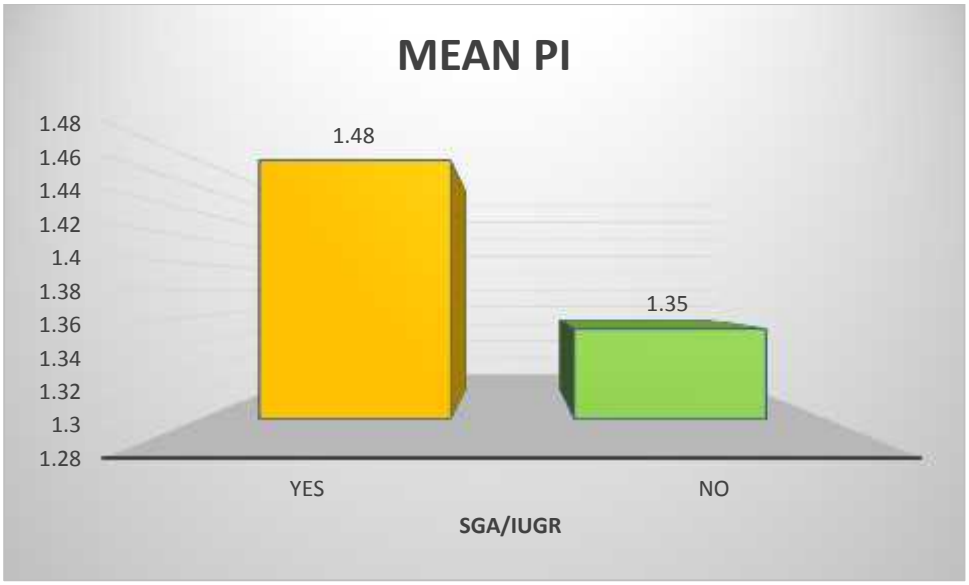
	PULSATILITY INDEX	
GEST AGE AT DELIVERY	MEAN	SD
PRE-TERM	1.51	0.17
TERM	1.35	0.14
P VALUE - 0.008		
SIGNIFICANT		
UNPAIRED T TEST		



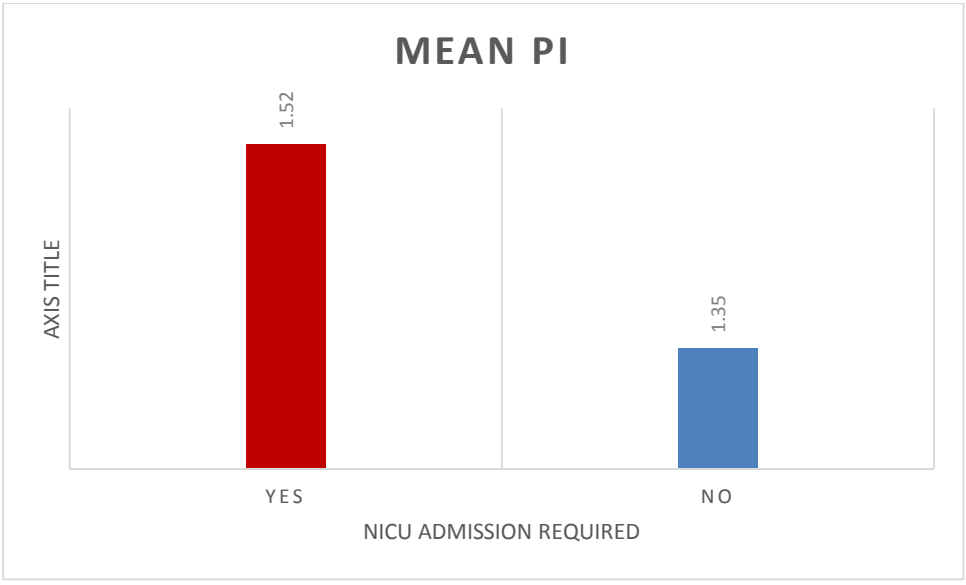
	PULSATILITY INDEX	
PREECLAMPSIA/PIH	MEAN	SD
PRESENT	1.46	0.18
ABSENT	1.37	0.15
P VALUE - 0.108		
NON SIGNIFICANT		
UNPAIRED T TEST		



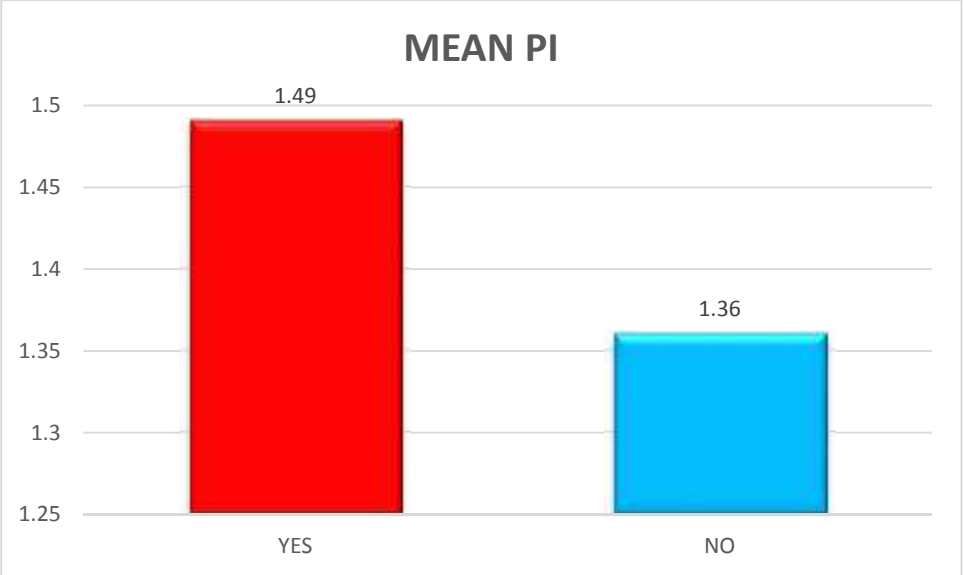
	PULSATILITY INDEX	
SGA / IUGR	MEAN	SD
YES	1.48	0.12
NO	1.35	0.14
P VALUE - 0.007		
SIGNIFICANT		
UNPAIRED T TEST		



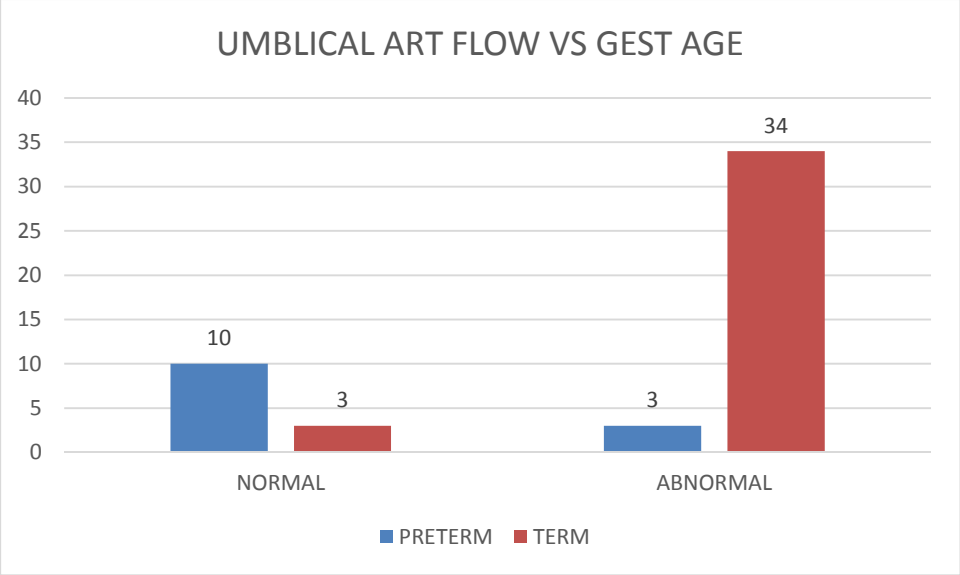
	PULSATILITY INDEX	
NICU ADMISSION REQUIRED	MEAN	SD
YES	1.52	0.18
NO	1.35	0.14
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		



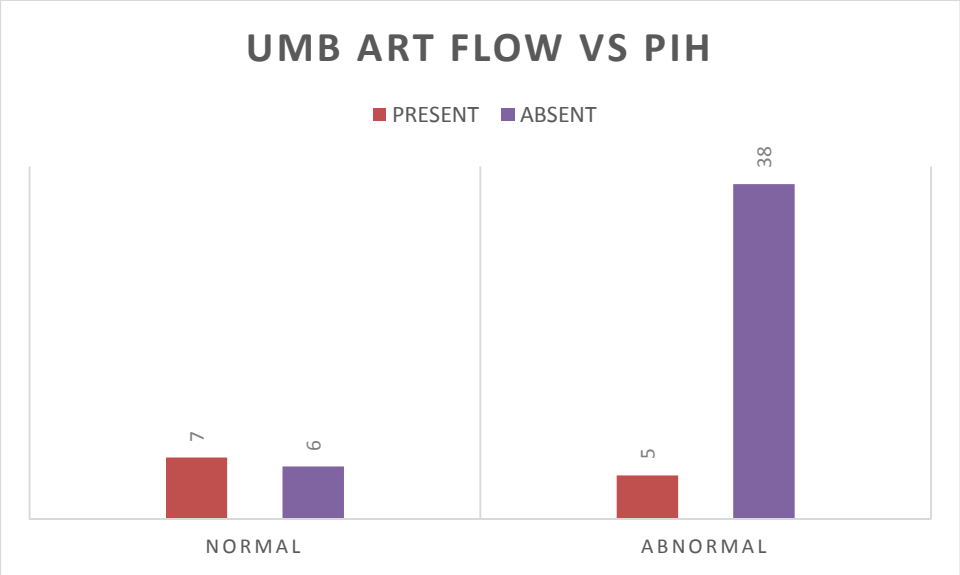
	PULSATILITY INDEX	
STEROID REQUIRED	MEAN	SD
YES	1.49	0.13
NO	1.36	0.16
P VALUE - 0.023		
SIGNIFICANT		
UNPAIRED T TEST		



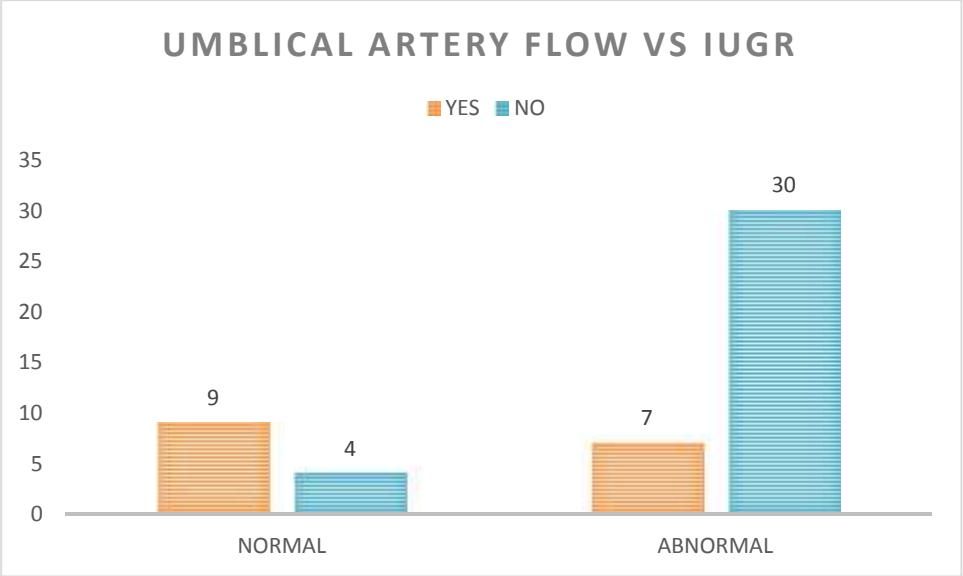
	UMBLICAL ARTERY FLOW	
GA AT DELIVERY	NORMAL	ABNORMAL
PRETERM	10	3
TERM	3	34
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 37.8		
CHI SQUARE TEST		



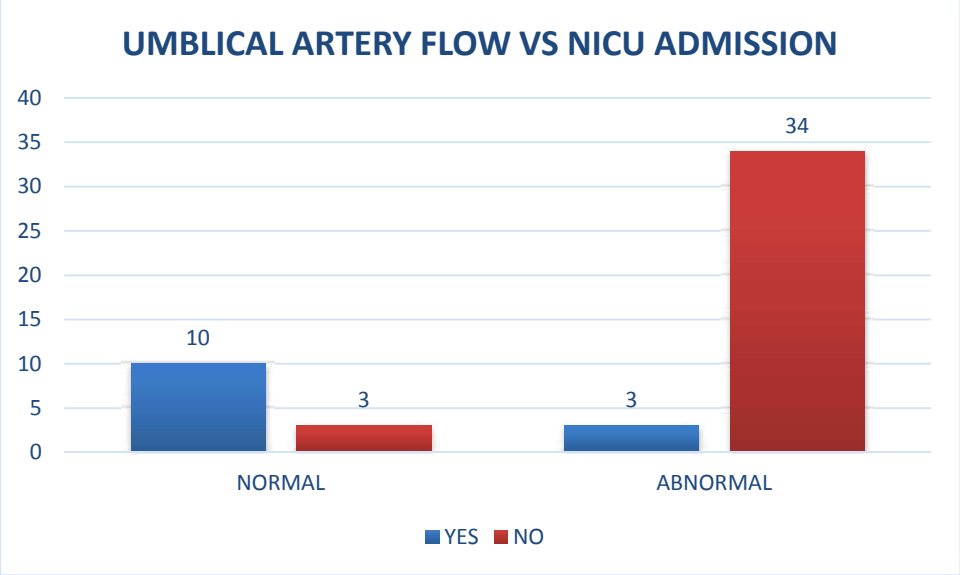
	UMBLICAL ARTERY FLOW	
PRE ECLAMPSIA/PIH	NORMAL	ABNORMAL
PRESENT	7	5
ABSENT	6	38
P VALUE - 0.003		
SIGNIFICANT		
ODDS RATIO - 7.46		
CHI SQUARE TEST		



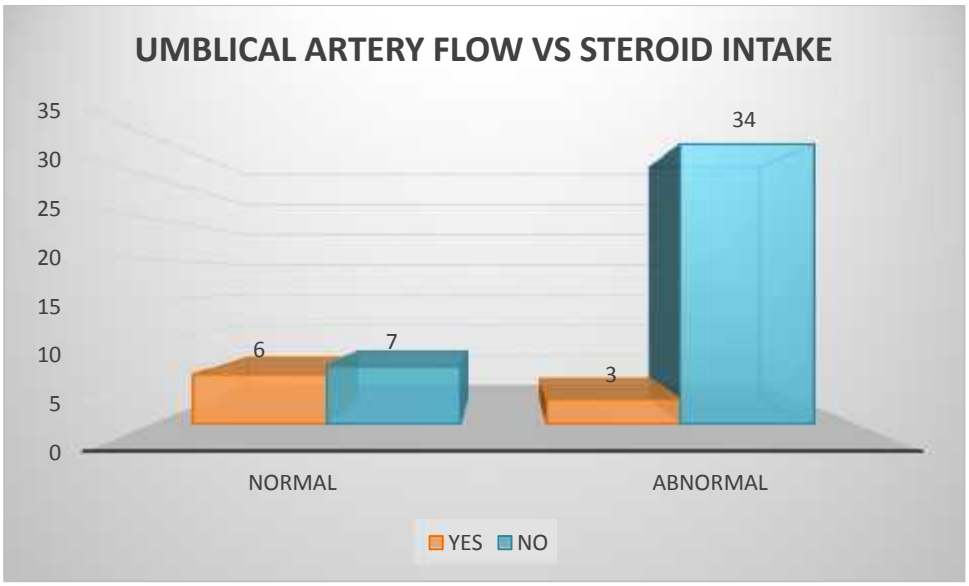
	UMBLICAL ARTERY FLOW	
SGA/IUGR	NORMAL	ABNORMAL
YES	9	7
NO	4	30
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 9.64		
CHI SQUARE TEST		



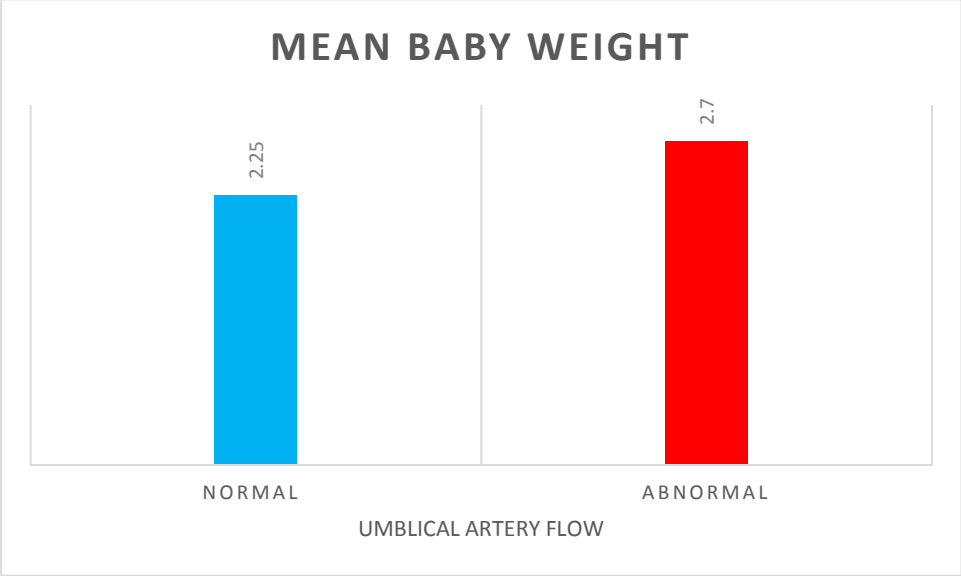
	UMBLICAL ARTERY FLOW	
NICU ADMISSION REQUIRED	NORMAL	ABNORMAL
YES	10	3
NO	3	34
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 37.77		
CHI SQUARE TEST		



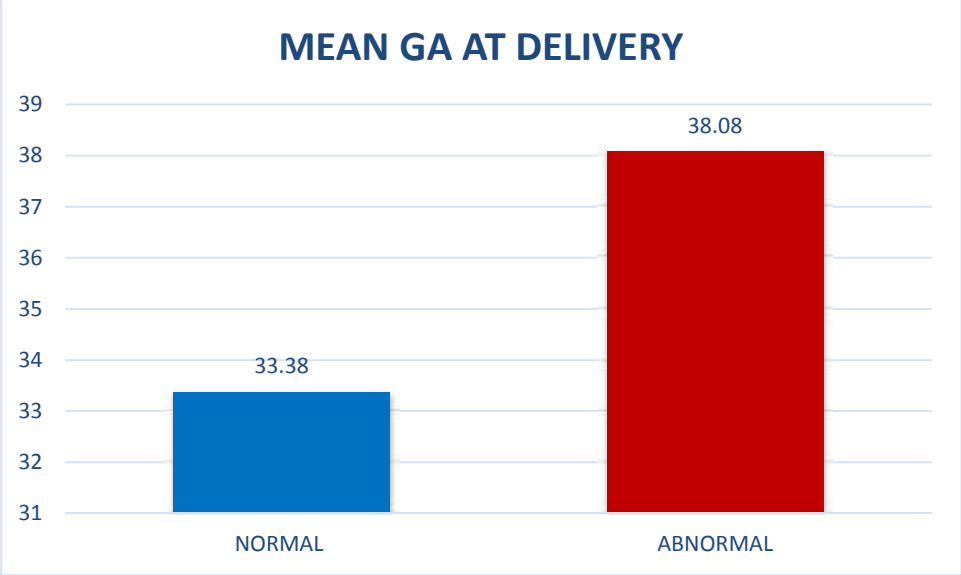
	UMBLICAL ARTERY FLOW	
STEROID REQUIRED	NORMAL	ABNORMAL
YES	6	3
NO	7	34
P VALUE - 0.002		
SIGNIFICANT		
ODDS RATIO - 9.7		
CHI SQUARE TEST		



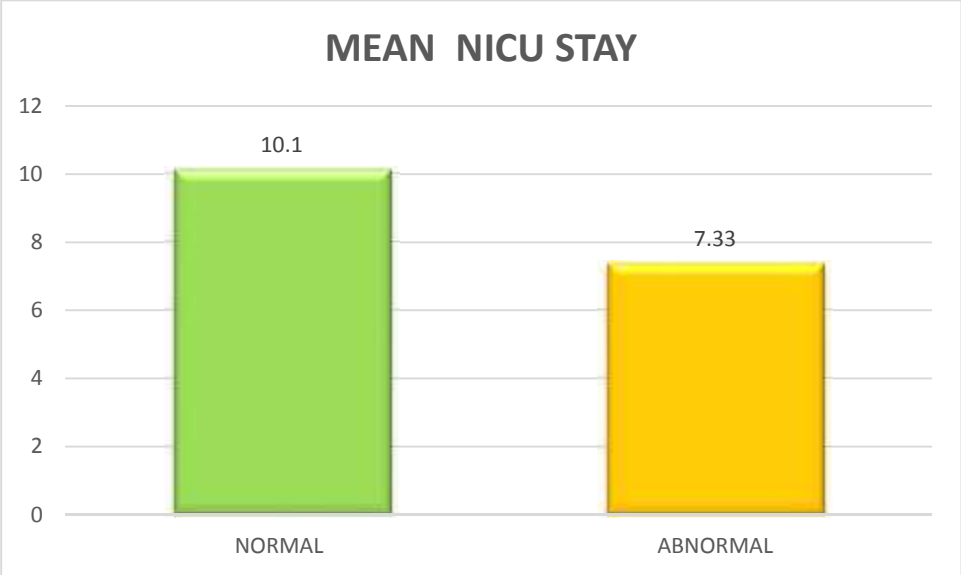
	BABY WEIGHT	
UMBLICAL ARTERY FLOW	MEAN	SD
NORMAL	2.25	0.54
ABNORMAL	2.7	0.39
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		



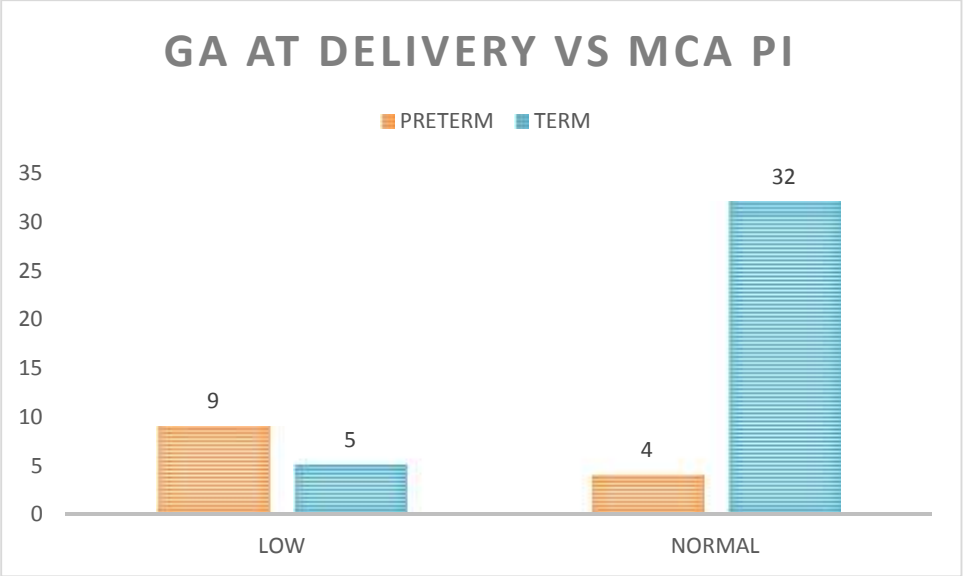
	GA AT DELIVERY	
UMBLICAL ARTERY FLOW	MEAN	SD
NORMAL	33.38	2.63
ABNORMAL	38.08	1.8
P VALUE - 0.002		
SIGNIFICANT		
UNPAIRED T TEST		



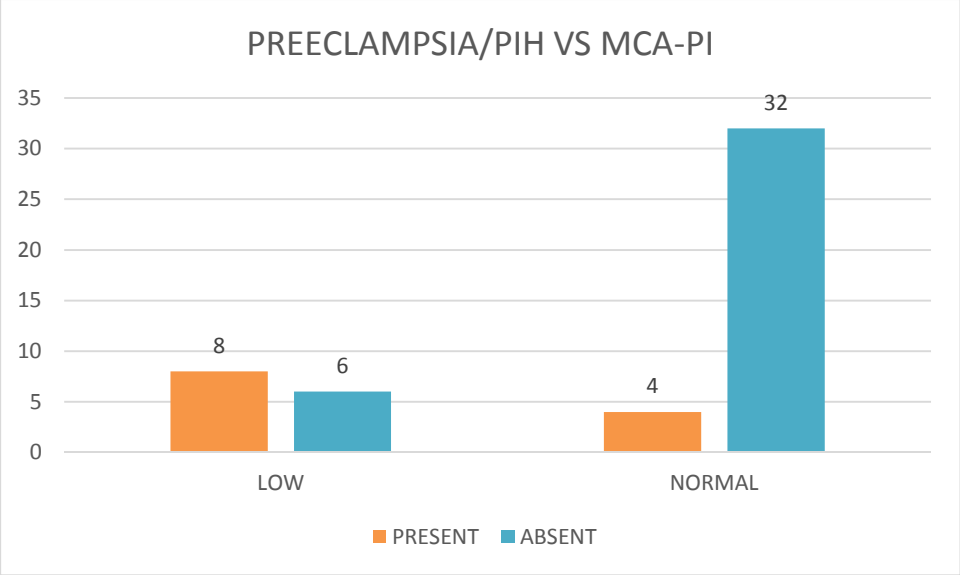
	NO OF DAYS IN NICU	
UMBLICAL ARTERY FLOW	MEAN	SD
NORMAL	10.1	3.1
ABNORMAL	7.33	1.8
P VALUE - 0.006		
SIGNIFICANT		
UNPAIRED T TEST		



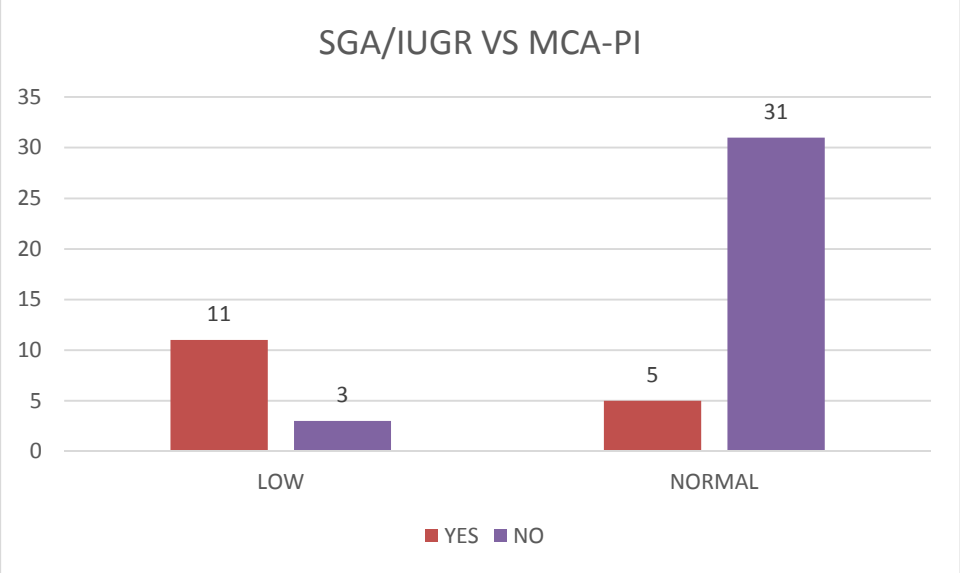
	MCA -PI	
GA AT DELIVERY	LOW	NORMAL
PRETERM	9	4
TERM	5	32
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 14.14		
CHI SQUARE TEST		



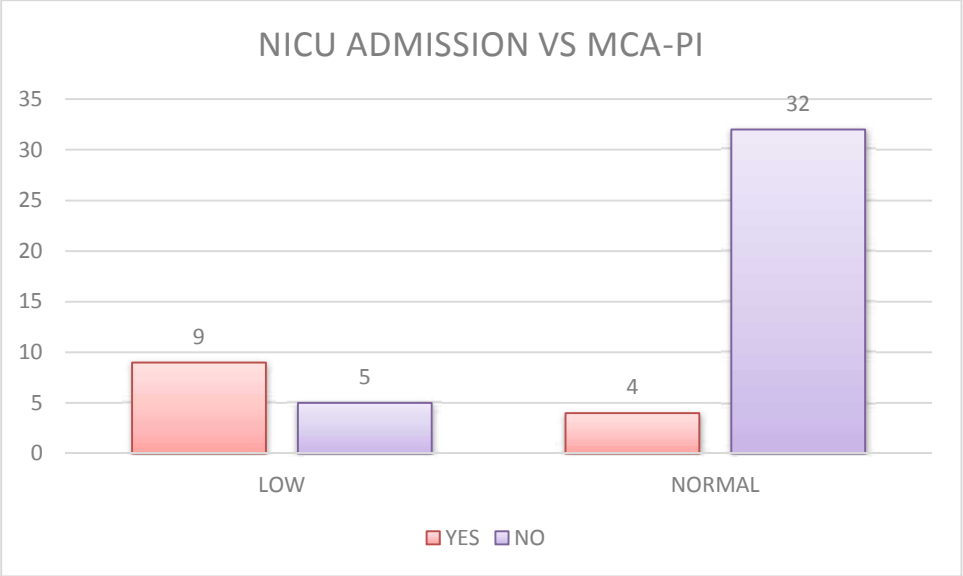
	MCA -PI	
PRE ECLAMPSIA/PIH	LOW	NORMAL
PRESENT	8	4
ABSENT	6	32
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 10.66		
CHI SQUARE TEST		



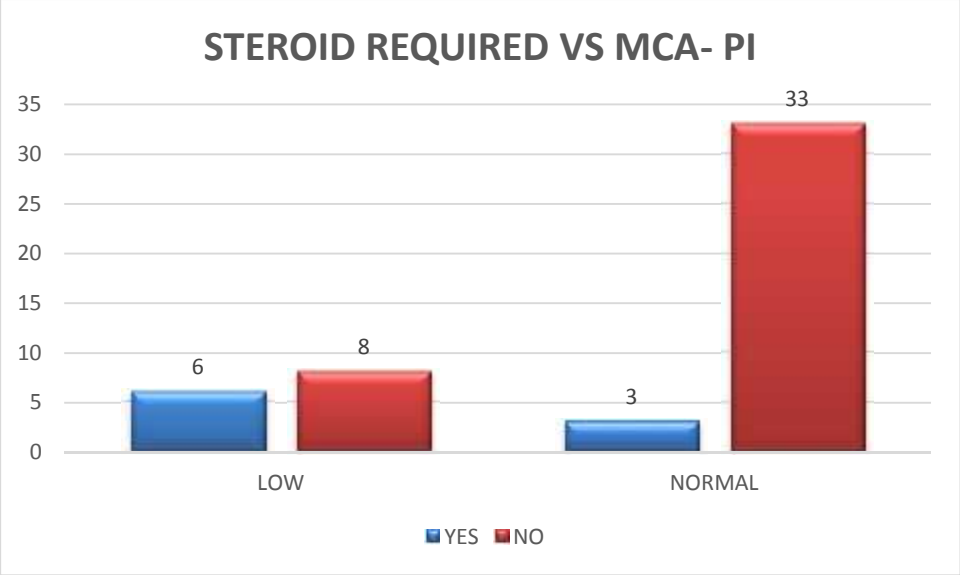
	MCA -PI	
SGA/IUGR	LOW	NORMAL
YES	11	5
NO	3	31
P VALUE - 0.000		
SIGNIFICANT		
ODDS RATIO - 22.7		
CHI SQUARE TEST		



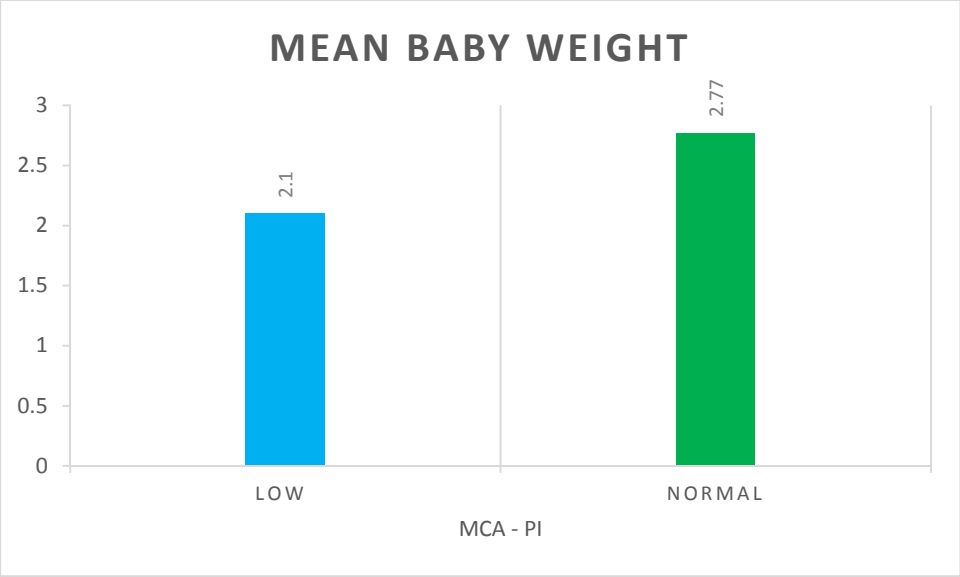
	MCA -PI	
NICU ADMISSION REQUIRED	LOW	NORMAL
YES	9	4
NO	5	32
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 14.4		
CHI SQUARE TEST		



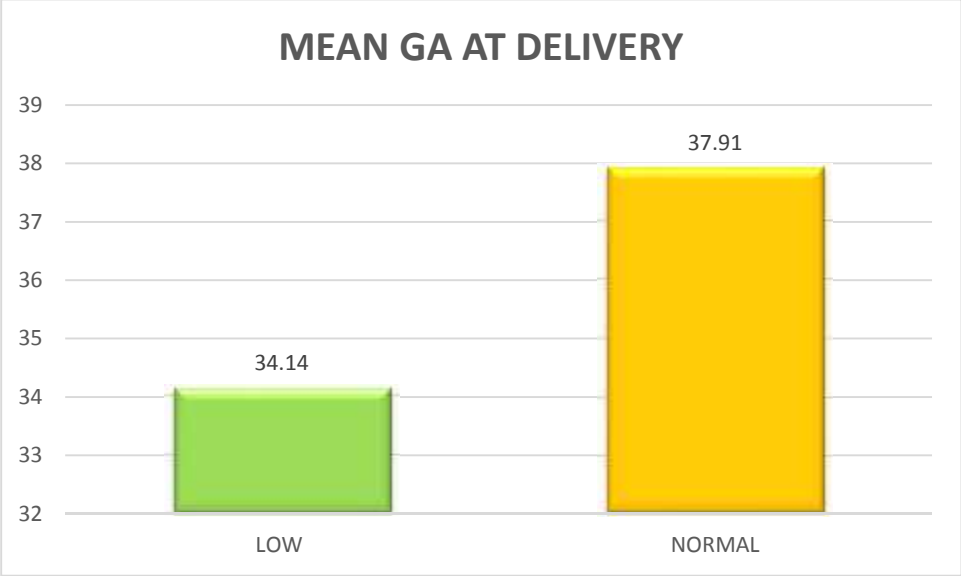
	MCA -PI	
STEROID REQUIRED	LOW	NORMAL
YES	6	3
NO	8	33
P VALUE - 0.004		
SIGNIFICANT		
ODDS RATIO - 8.25		
CHI SQUARE TEST		



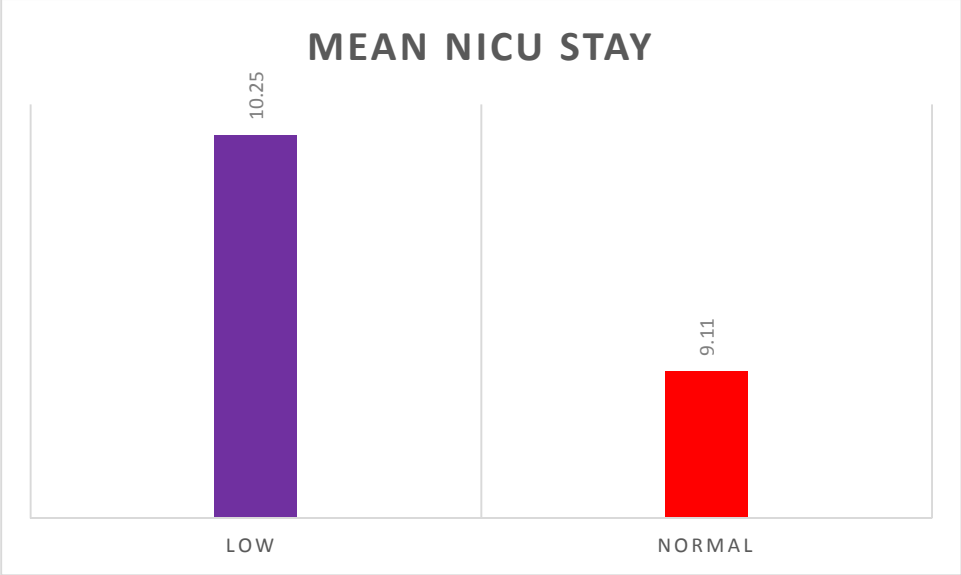
	BABY WEIGHT	
MCA-PI	MEAN	SD
LOW	2.1	0.4
NORMAL	2.77	0.35
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		



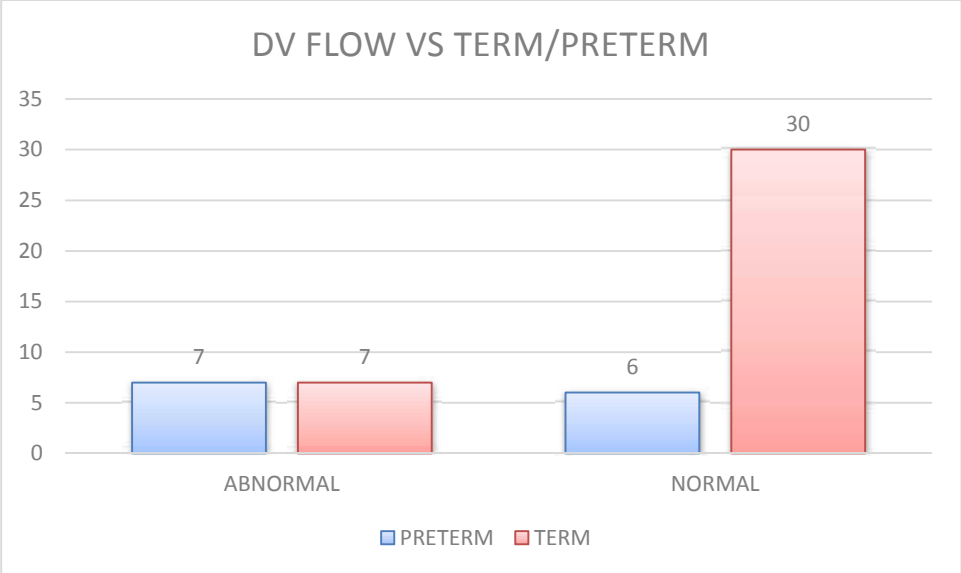
	GA AT DELIVERY	
MCA-PI	MEAN	SD
LOW	34.14	3.1
NORMAL	37.91	2.01
P VALUE - 0.004		
SIGNIFICANT		
UNPAIRED T TEST		



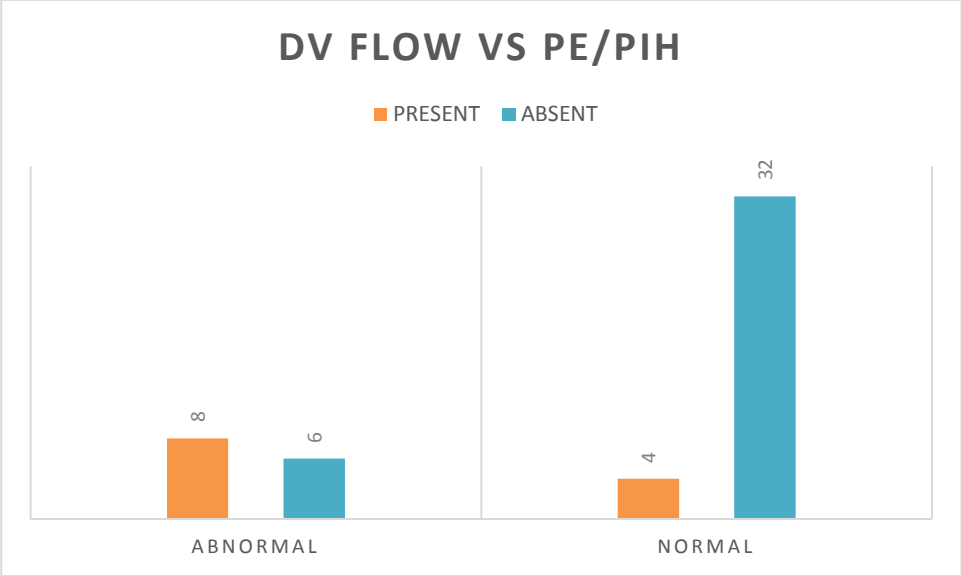
	NO OF DAYS IN NICU	
MCA-PI	MEAN	SD
LOW	10.25	3.2
NORMAL	9.11	1.7
P VALUE - 0.031		
SIGNIFICANT		
UNPAIRED T TEST		



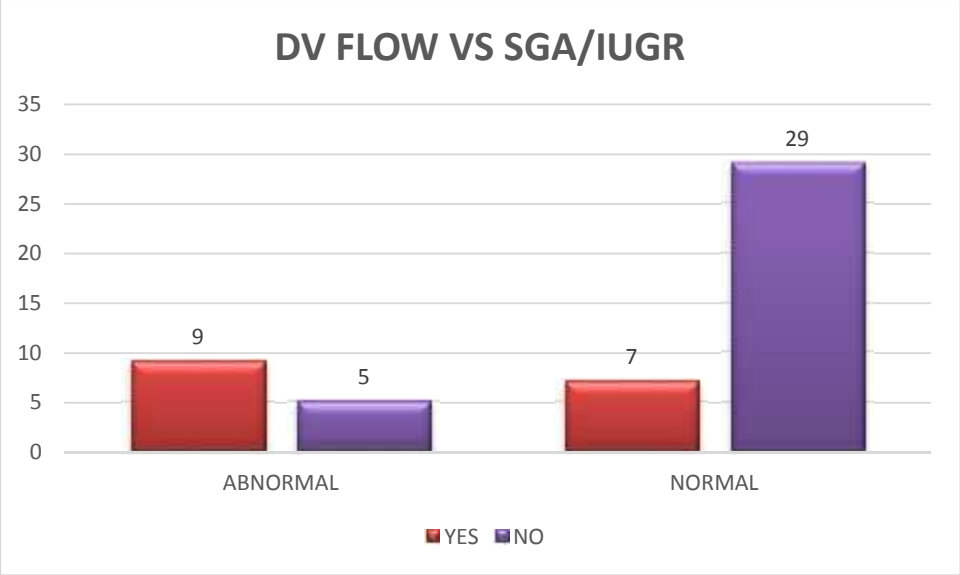
	DUCTUS VENOSUS FLOW	
GA AT DELIVERY	ABNORMAL	NORMAL
PRETERM	7	6
TERM	7	30
P VALUE - 0.016		
SIGNIFICANT		
ODDS RATIO - 5		
CHI SQUARE TEST		



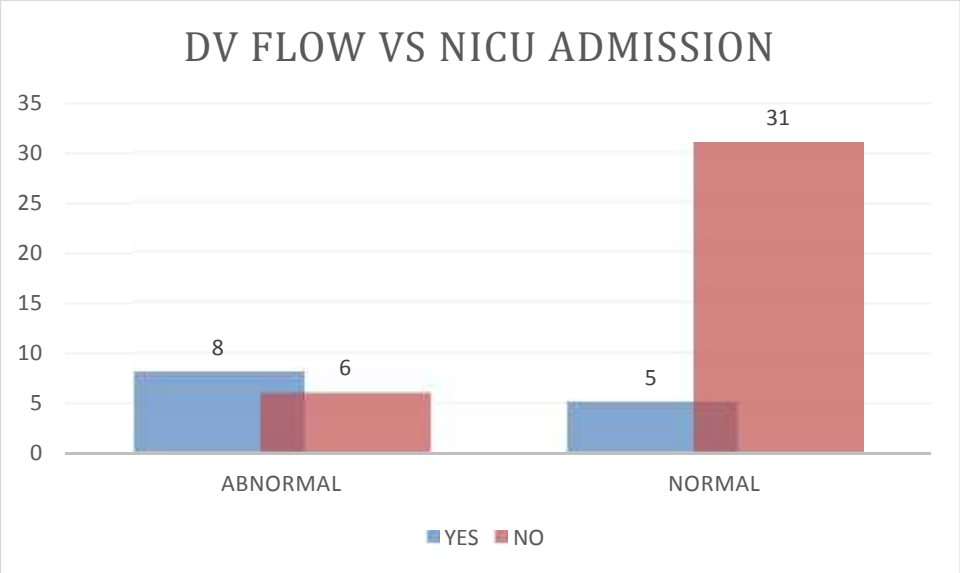
	DUCTUS VENOSUS FLOW	
PRE ECLAMPSIA/PIH	ABNORMAL	NORMAL
PRESENT	8	4
ABSENT	6	32
P VALUE - 0.001		
SIGNIFICANT		
ODDS RATIO - 10.6		
CHI SQUARE TEST		



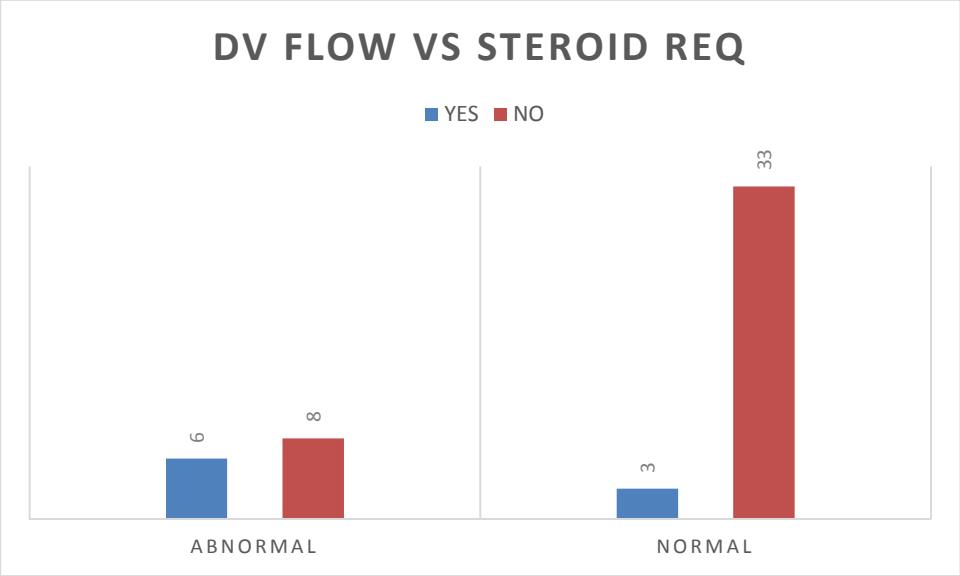
	DUCTUS VENOSUS FLOW	
SGA/IUGR	ABNORMAL	NORMAL
YES	9	7
NO	5	29
P VALUE - 0.002		
SIGNIFICANT		
ODDS RATIO - 7.45		
CHI SQUARE TEST		



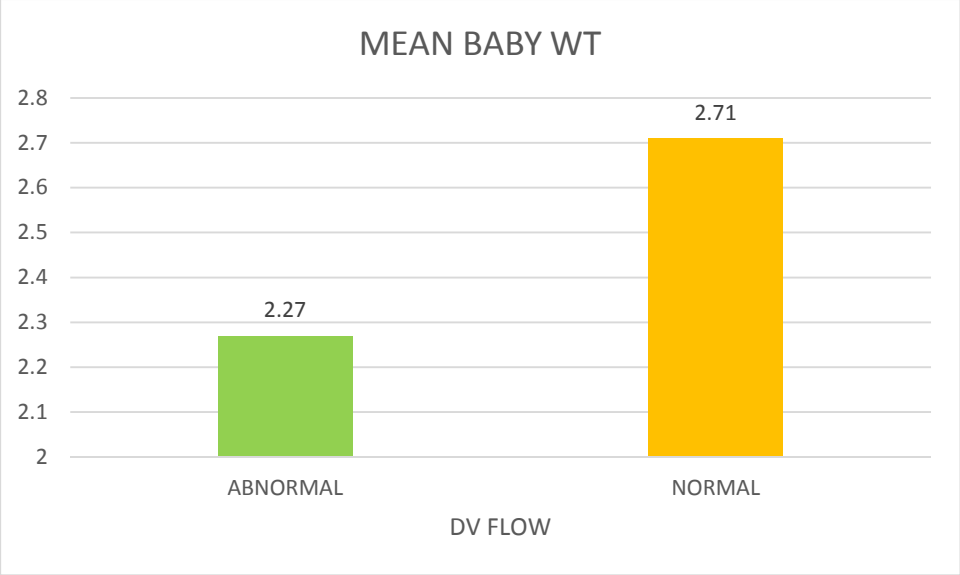
	DUCTUS VENOSUS FLOW	
NICU ADMISSION REQUIRED	ABNORMAL	NORMAL
YES	8	5
NO	6	31
P VALUE - 0.002		
SIGNIFICANT		
ODDS RATIO - 8.26		
CHI SQUARE TEST		



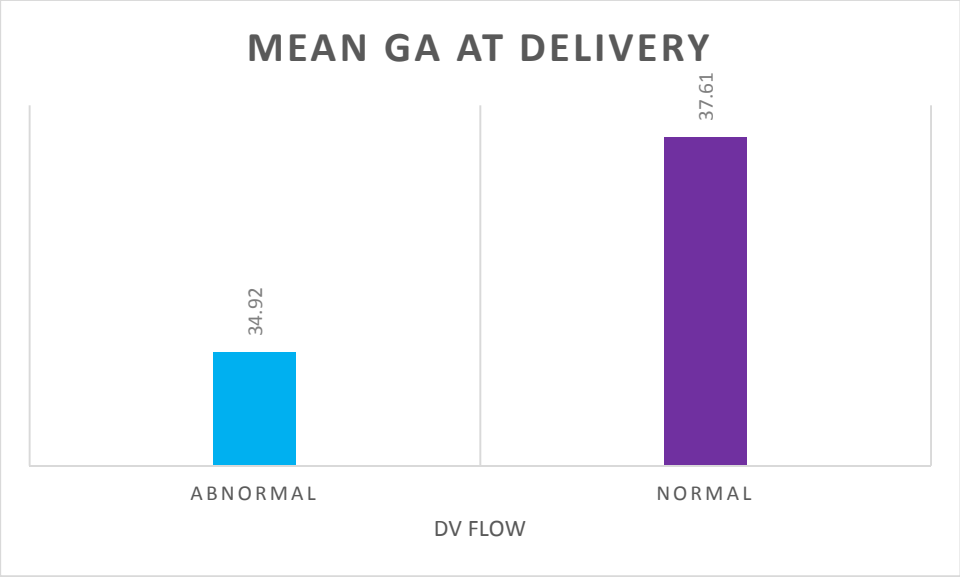
	DUCTUS VENOSUS FLOW	
STEROID REQUIRED	ABNORMAL	NORMAL
YES	6	3
NO	8	33
P VALUE - 0.004		
SIGNIFICANT		
ODDS RATIO - 8.26		
CHI SQUARE TEST		



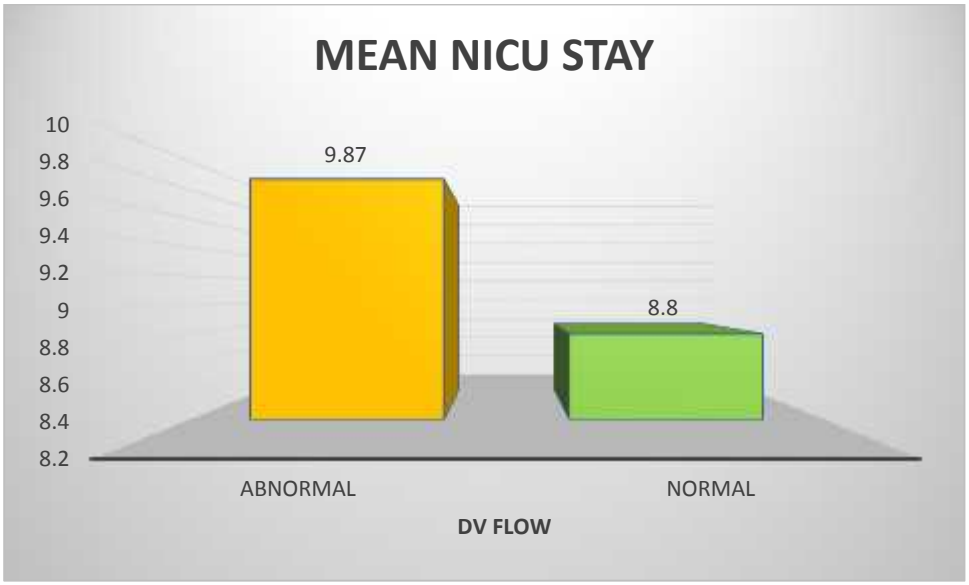
	BABY WEIGHT	
DUCTUS VENOSUS FLOW	MEAN	SD
ABNORMAL	2.27	0.55
NORMAL	2.71	0.38
P VALUE - 0.002		
SIGNIFICANT		
UNPAIRED T TEST		



	GA AT DELIVERY	
DUCTUS VENOSUS FLOW	MEAN	SD
ABNORMAL	34.92	3.26
NORMAL	37.61	2.39
P VALUE - 0.002		
SIGNIFICANT		
UNPAIRED T TEST		



	NO OF DAYS IN NICU	
DUCTUS VENOSUS FLOW	MEAN	SD
ABNORMAL	9.87	3.2
NORMAL	8.8	1.7
P VALUE - 0.045		
SIGNIFICANT		
UNPAIRED T TEST		



DISCUSSION

This study was primarily done to evaluate whether abnormal Doppler finding at 20 – 22 weeks of gestational period is useful in predicting the development of IUGR, pre-eclampsia, eclampsia, preterm delivery, NICU admission, steroid requirement.

In this study, 50 pregnant women in gestational age of 20-22 weeks who have a reduced sympysio-fundal height to less than 10^{th} percentile were selected. They were assessed with Doppler velocimetry, Follow up of all the patients were done. The period between 20 -22 weeks was chosen to perform the Doppler because a routine anomaly scan was done regularly in all pregnant mothers during that period. Coming to age distribution of the patient only 14% (N=7) cases where above 30 years while most of cases were between 20- 30 yrs. Among our study group around 24(48%) mothers were primi while others have history of previous child birth.

Before going in deep about doppler findings let’s see prevalence of adverse outcomes in our study group. Among 50 patients in our study group 13 patients (26%) delivered preterm before 36 weeks of gestation 12(24%) of 50 mothers in our study group developed preeclampsia or pregnancy induced hypertension at some point of time in their pregnancy.

Pregnant mothers in our study group delivered around 16 babies (32%) with either SGA or IUGR. While 13(26%) of neonates delivered required admission in NICU for some reason. Among those neonates 12(24%) required

steroids as a part of treatment during their stay in NICU which clearly proves that lung maturity would not be there as a effect of pretem or IUGR in those neonates.

In our study group the Doppler findings were as follows. To start with evaluation of uterine artery. It has been shown in the previous studies and in the present study, elevated uterine artery pulsatility index and presence of diastolic notch was significantly associated with developing IUGR and other adverse outcomes.

In our study group during Doppler study of uterine artery diastolic notch was present in 13(26%) patients and pulsatility index was above 1.45 in 17(34%) patients.

Coming To the evaluation of umbilical artery we analysed the end diastolic flow where reverse, absence or slow end diastolic flow was considered abnormal which was seen in 13 patients. In Middle cerebral artery we assessed the pulsatility index and if PI is less than 1.7 we take it as low and was found in 14(28%) of patients. Ductus Venous was assessed based on the waveforms. If waveform is reverse, slow or absent we considered it as abnormal and was seen in 14(28%) of patients in our study group.

We analysed the above findings with various maternal and perinatal outcomes, with 100% follow up rate. The factors like development of PIH or preeclampsia, IUGR/SGA neonates, term or preterm delivery, requirement of admission in NICU, Steroid requirement were correlated. We also analysed the

impact of Doppler indices on mean gestational age at delivery, mean baby weight after delivery, and mean number of days stay in NICU.

To start with evaluation of uterine artery we analysed both presence of diastolic notch and pulsatility index with parameters. We first analysed the gestational age at delivery, among 13 patients who had diastolic notch 8 babies were delivered preterm. This relationship is significant with an odds ratio of 10.24 which shows babies with presence of diastolic notch has ten times higher risk of preterm delivery compared to absence of diastolic notch.Even the mean difference of gestational age in weeks compared using unpaired T test was also significant with P value of 0.004

Pre-eclampsia or PIH developed in seven patients among 13 with diastolic notch. With an odds ratio of 7.46 those mothers with persistent diastolic notch has seven to eight time's higher risk of developing preeclampsia or PIH.

Coming to the important aspect of our study the impact of these indices on IUGR. Among our patients nine among 13 mothers having persistent diastolic notch ended up in delivering IUGR or SGA babies which was also statistically significant with odds ratio of 9.64 they had ten times higher risk. The mean difference in baby weight was compared using unpaired T test and was also significant with p value less than 0.05

Similarly babies delivered with persistent diastolic notch in Doppler also ended up requiring NICU admission and steroid requirement, both were

statistically significant with a higher odds ratio. Even the mean number of days stay in NICU was higher in patient with persistent diastolic notch.

In a previous research done Becker R and Vonk R, uterine artery Doppler results at 20-23 weeks of gestation and adverse obstetric outcomes were evaluated.[10] They evaluated the diagnostic value of Doppler sonography of the uterine arteries at 20-23 weeks as a screening method in a low-risk population. They evaluated uterine artery impedance using the mean PI of the left and right arteries or diastolic notching as primary markers. The outcome parameters were pre-eclampsia, IUGR, intrauterine/neonatal death, and preterm delivery, before 32 weeks. They showed a clear relationship between the elevation of PI and the frequency of adverse pregnancy outcomes, with the frequency of complications varying from 3.2 to 38.4%.This is similar to our results though our study group patients were of high risk for IUGR which proves the significance of uterine artery as an important indices in assessing the maternal and foetal outcome.9 (Barati M, Shahbazian N et al)

We next evaluated the impact of pulsatility index of uterine artery on the foetal and maternal sequelae by two ways. First by grouping the patients with pulsatility index cut off taken as 1.45 as mean for 20-22 wks. from previous studies. To start with the gestational age at delivery, among 17 patients who had pulsatility index above 1.45 ten babies were delivered preterm. This relationship is significant with an odds ratio of 14.28 which shows babies with higher uterine artery PI has approximately 14 times higher risk of preterm delivery compared to

lower pulsatilty index. We also evaluated the mean difference of gestational age in weeks using unpaired T test was also significant with P value of 0.002

Pre-eclampsia or PIH developed in seven patients among 17 with pulsatility index more than 1.45. Though this is less in total patients with high PI, when compared to number of patients with PIH with normal UA_PI its high and statistically significant. With an odds ratio of 3.92 those mothers with higher PI has around 4 time's higher risk of developing preeclampsia or PIH.

Coming to the important aspect of our study the impact of these indices on IUGR. Among our patients ten among 17 mothers having high PI ended up in delivering IUGR or SGA babies which was also statistically significant with odds ratio of 6.42 they had approximately 6 to 7 times higher risk. The mean difference in baby weight was compared using unpaired T test and was also significant with p value less than 0.05.

Similarly babies delivered with high pulsatility index in Doppler also ended up requiring NICU admission and steroid requirement, both were statistically significant with a higher odds ratio. Even the mean number of days stay in NICU was higher in patient with persistent diastolic notch which was analysed using the unpaired t test.

We also analysed the mean difference of pulsatility index numerically over the maternal and foetal outcome using unpaired T test which showed there is significant difference in the mean pulsatility index in relation to parameters like term/preterm, IUGR, requirement of NICU admission and steroid

requirement all had a higher mean PI with statistical significance except for development of PIH or pre-eclampsia where it was not statistically significant with P value of 0.108.

Next analysis was done for umbilical artery. We analysed the end diastolic flow in Umbilical artery. Reverse flow, absence of flow or decreases flow were considered abnormal and was analysed. Starting with the gestational age at delivery, among 13 patients who had abnormal UA -EDF 10 babies were delivered preterm. This relationship is significant with an odds ratio too high of 37.8 which shows babies with presence of abnormal flow in umbilical artery has around 38 times higher risk of preterm delivery compared to mothers with normal UA-EDF. Even the mean difference of gestational age in weeks compared using unpaired T test was also significant with P value of 0.002 where in abnormal flow patients gestation age at delivery was earlier.

Pre-eclampsia or PIH developed in seven patients among 13 with abnormal EDF, With an odds ratio of 7.46 those mothers with abnormal flow has seven to eight time's higher risk of developing preeclampsia or PIH.

Our main objective of study to know the influence of these Doppler indices on IUGR. Among our patients nine among 13 mothers having abnormal flow delivered IUGR or SGA babies, this was statistically significant with odds ratio of 9.64 which shows they had ten times higher risk. The mean difference in baby weight was also analysed using unpaired T test and was also significant with p value less than 0.05

Similarly babies delivered with abnormal end diastolic flow in umbilical artery also ended up requiring NICU admission and steroid requirement, both were statistically significant with an higher odds ratio. Even the mean number of days stay in NICU was higher in patient with abnormal flow.

An previous study done taking the same objective as ours explained and showed that in the 50 patients they studied those who are with abnormal umbilical artery Doppler, 15 patients had IUGR births with a sensitivity of 25% and 42.86% for S/D ratio and RI, respectively. It is similar to opinion by Antsaklis et al and Beattie et al. Romero et al studied 43 women, and among them, 52% had abnormal umbilical Doppler. They found that abnormal umbilical Doppler is associated with lower birth weight, lower Apgar score, and significant neonatal morbidity. These findings and prevalence of IUGR were similar to our studies with 14 patients having IUGR which further insist the importance of umbilical artery Doppler status on future outcomes

The next analysis was done by using the Pulsatility index of middle cerebral artery where PI less than 1.7 was considered abnormal. We first analysed the gestational age at delivery, among 14 patients who had low PI nine babies were delivered preterm. This relationship is significant with an odds ratio of 14.14 which shows babies with low PI in MCA has around 14 times higher risk of preterm delivery compared to normal MCA-PI. Even the mean difference of gestational age in weeks compared using unpaired T test was also significant with P value of 0.004

Pre-eclampsia or PIH developed in eight patients among 14 with low MCA-PI With an odds ratio of 10.66 mothers with MCA–PI less than 1.7 ten time's higher risk of developing pre-eclampsia or PIH.

Among our patients eleven among 14 mothers having persistent low MAC -PI ended up in delivering IUGR or SGA babies which was also statistically significant with an higher odds ratio of 22.7. The mean difference in baby weight was also analysed using unpaired T test and was also significant with p value less than 0.05.

Similarly babies delivered with low MCA-PI also ended up requiring NICU admission and steroid requirement, both were statistically significant with an higher odds ratio. Even the mean number of days stay in NICU was more in patient with low MCA-PI.

Very minimal studies have proved that middle cerebral artery peak systolic velocity may be a better predictor of perinatal mortality in preterm IUGR than the PI, but additional study is needed to confirm this finding.17 When there is foetal hypoxemia, there will be brain-sparing reflex, which is specified by increased end-diastolic flow velocity which is indicated by a low PI in the middle cerebral artery14.This hypothesis is what seen in our study where a low PI has in middle cerebral artery has an higher impact on maternal and fetal outcome hence showing need to evaluate the MCA using Doppler velocimetry.

Finally we analysed the ductus venosus flow and reverse or slow or absent wave form were considered abnormal. Gestational age at delivery was analysed

and among 14 patients who had abnormal waveform nine babies were delivered preterm. This relationship is significant with an odds ratio of 10.6 which shows babies with abnormal flow in ductus venosus has ten times higher risk of preterm delivery compared to normal flow. Even the mean difference of gestational age in weeks compared using unpaired T test was also significant with P value of 0.002

Pre-eclampsia or PIH developed in eight patients among 14 with abnormal ductus venosus flow. With an odds ratio of 10.6 those mothers with abnormal DV flow has approximately ten time's higher risk of developing preeclampsia or PIH.

Coming to the important aspect of our study the impact of these indices on IUGR. Among our patients nine among 14 mothers having abnormal flow ended up in delivering IUGR or SGA babies which was also statistically significant with odds ratio of 7.45 they had seven times higher risk. The mean difference in baby weight was compared using unpaired T test and was also significant with p value less than 0.05.

Similarly babies delivered with abnormal DV flow in Doppler also ended up requiring NICU admission and steroid requirement, both were statistically significant with a higher odds ratio. Even the mean number of days stay in NICU was higher in patient with abnormal ductus venosus flow.

Abnormalities in ductus venosus Doppler waveforms are sensitive tools for the evaluating foetal well-being specifically before 32 weeks' gestation, and

may help to modify our decision-making in regard to time of delivery in affected foetuses. It is a more direct indicator for hemodynamic performance. Baschat et al. indicated that abnormal DV-PI proved to be the best interpreter of poor neonatal outcome in severe IUGR which was in accordance with the present study. Baschat et al. and Schwarze et al. also stated that pulsation in the UV followed by waveform abnormalities in the DV was the most sensitive Doppler parameter for identifying foetuses at risk for stillbirth, perinatal or neonatal death and IUGR.This results are similar to that of our study which proves our hypothesis.

CONCLUSION

After analysing results of our study we are of the conclusion that Doppler velocimetry can be used as routine check-up, follow up in high risk pregnancy suspected of IUGR, to help management and control of IUGR. Doppler ultrasound is a must to pregnant women who have any complications to detect the IUGR, thus foetal problem could be avoided. Early screening of the UA Artery and MCA waveform should be performed along either uterine artery and ductus venosus analysis as all indices have positive relation with maternal and neonatal outcomes particularly IUGR and a proper early diagnosis of IUGR and may decrease the foetal and maternal morbidity and mortality rate. The limitation of our study is sample size hence it would be better to do further studies by having a large sample and further modalities, and also combining all Doppler indices with other tests that are related to IUGR used in clinical care, this may improve the predictive accuracy and the clinical important value of the tests. This study can further insight on accuracy of prediction of IUGR by comparing the indices with patient in low risk groups.

BIBLIOGRAPHY

1.Alan, H.D and N. Lauren, Current Obsretric and Gynecologyic: Diagnostic and Treatment. 10 ed2003, USA:McGraw-Hill.

2. Asim Kuorjak, Frank A Cherven. Text book of ultrsound of gynecology and obstetric. 1st ed. Medical publisher (P) LTD. New delhi. 2006.

3.John,C,H.,Obstetric Ultrasound:Artistry in Practice.1st ed,2008,U.S:John Wiley&Sons.

4. Arey LB: Developmental Anatomy: A text book and labrotary manual of Embryology.7th ed. philadelphia 2011

5. Jane A Bates et al Differentiation of growth retarded from normally grown foetuses and prediction of intrauterine growth retardation using Doppler ultrasound BJOG 1996 ;103(7) ;670-675

6. Williams KP, Farquharson DF, Bebbington M, Danscreau J, Galerneau F, Wilson RD, et al. Screening for fetal well-being in a high-risk pregnant population comparing the nonstress test with umbilical artery Doppler velocimetry: A randomized controlled clinical trial. Am J Obstet Gynecol. 2003;188(5):1366-1371. (Level II evidence)

7.Williams, R.L., Creasy, R.K., Cunningham, G.C., Hawes, W.E., Norris, F.D. and Tashiro, M. 1982 Fetal growth and perinatal viability in California. Obstetrics and Gynecology 59, 62432

8.WHO 1995 Expert Committee Report: Physical status: the use and interpretation of anthropometry. Technical Report Series 854.Geneva: World Health Organization.

9. Krebs, C., V.L. Giyanani, and R.L. Eisenberg, Ultrasound atlas of vascular diseases1999, U.S: Appleton & Lange.

10. Coleman MM, Spear ML, Finkelstein M, et al: Short_Term use of umbilical artery catheters may not be associated with increasd risk of thrombosis. Pediatrics 2004 APR;113(4):770-4

11. Lugo G, Cassady G: Intrauterine growth retardation. Clinicopathologic findings in 233 consecutive infants. Am J Obstet Gynecol 133:281, 1991.

12. Lausman A, McCarthy FP, Walker M, Kingdom J. Screening, diagnosis, and management of intrauterine growth restriction. J Obstet Gynaecol Can. 2012;34(1):17-28.

13. Scott KE, Usher R: Fetal malnutrition: Its incidence, causes and effects. Am J Obstet Gynecol 94:951,1996.

14. Stampalija T, Gyte GM, Alfirevic Z. Utero-placental Doppler ultrasound for improving pregnancy outcome. Cochrane Database Syst Rev. 2010 (9):CD008363. (Level II evidence)

15. Lugo G, Cassady G: Intrauterine growth retardation. Clinicopathologic findings in 233 consecutive infants. Am J Obstet Gynecol 133:281, 1991.

16. Vandenbosche, R.C. and J.T. Kirchner, Intrauterine growth retardation. Am Fam Physician, 1998. 58(6): p. 1384-90, 1393-4.

17. Smith-Bindman R, Chu PW, Ecker JL, Feldstein VA, Filly RA, Bacchetti P. US evaluation of fetal growth: prediction of neonatal outcomes. Radiology. 2002;223(1):153-61

18. P. Cox and T. Marton, “Pathological assessment of intrauterine growth restriction,” Best Practice and Research: Clinical Obstetrics and Gynaecology, vol. 23, no. 6, pp. 751–764, 2009.

19. D. G. Jang, Y. S. Jo, S. J. Lee, N. Kim, and G. S. R. Lee, “Perinatal outcomes and maternal clinical characteristics in IUGR with absent or reversed end-diastolic flow velocity in the umbilical artery,” Archives of Gynecology and Obstetrics. In press.

20. Smith GC, Yu CK, Papageorghiou AT, Cacho AM, Nicolaides KH. Maternal uterine artery Doppler flow velocimetry and the risk of stillbirth. Obstet Gynecol. 2007;109(1):144-51

21. Thornton JG, Hornbuckle J, Vail A, Spiegelhalter DJ, Levene M. Infant wellbeing at 2 years of age in the Growth Restriction Intervention Trial (GRIT): multicentred randomised controlled trial. Lancet. 2004;364(9433):513-20.

22. Bakketeig, L. S. and Hoffman, H. J. (1983), The Tendency to Repeat Gestational Age and Birth Weight in Successive Births, Related to Perinatal Survival. Acta Obstetricia et Gynecologica Scandinavica, 62: 385–392.

23. WHO International collaborative study of Hypertensive disorders of pregnancy .Geographic variation in the incidence of Hypertension in pregnancy. Am J. Obstet. Gynecol.1998; 158 :80-83.

24.Confidential Enquiry into maternal Deaths : Why mothers die? 2000-2002. The confidential Enquiries into maternal deaths in U.K. London : RCOG Press; 2004.

25.Faraq K , et al . Prediction of preeclampsia .Obstet Gynecol Surv 2004 ; 59:464 -482.

26. William Obstetrics 24th edition Table 40-2. page no.730.

27. Dekkar GA, et al . Etiology and pathogenesis of pre-eclampsia . Am J Obstet Gynecol 1998; 179:1359-1375.

28..Durnwald C, Mercer B.A prospective comparison of total protein/creatinine ratio versus 24-hour urine protein in women with suspected preeclampsia.Am J Obstet Gynecol. 2003 Sep;189(3):848-52

29. . Duckitt K , et al. Risk factors for pre-eclampsia at antenatal booking: Systematic Review of Controlled studies BMJ 2005; 330: 565-577.

30.Gary Cunningham et al. Hypertensive disorders in pregnancy. Williams' Textbook of Obstetrics, 22nd Edition; 34:778-780.

31. Khong et al. Immunologic demonstration of endothelial disruption in acute atherosis in pre-eclampsia. European journal of Obstet and Gynecol and Reproductive Biology 1993; 51: 193-197.

32.Dekker G et al . Primary, secondary and tertiary prevention of pre-eclampsia.Lancet 2001;357:209-215.

33.Allen C, et al. Bed rest: a potentially harmful treatment needing more care evaluation .Lancet 1999; 354: 1229-1233.

34. Marcoux S, et al. Job strain and pregnancy induced hypertension. Epidemiology 1999;354:1229-1233.

35.Steegers EA, et al . Dietary Sodium restriction during pregnancy : a historical review. Eur J obstet and gynecol Reprod Biol . 1991; 40:83-90

36. Kramer MS. Energy / protein restriction for high weight for height or weight gain during pregnancy. N England J Med 1997;336:1117-1124.

37. Oslen S, et al. Randomised clinical trials of fish oil supplementation in high risk pregnancies. Br. J Obstet Gynecol 2000; 107 : 382-395.

38.Royal College of Obstetricians and Gynaecologists alcohol consumption in pregnancy. Guideline Report 9. London, Royal College of Obstetrics and Gynecologists,1996.

39. Ekerhovd E. Dietary supplementation with L- arginine in women with pre-eclampsia . Acta Obstet Gynecol Scand 2004 ; 83:871-872.

40.Sibai BM, Treatment of hypertension in pregnant women. N Engl J Med 1996 ; 335 : 257-265.

41. Jonsson B, et al. Zinc supplementation during pregnancy : a double blind randomised clinical trial. Acta Obstet Gynecol Scand 1996;75:725-729.

42. Makrides M, et al . Magnesium supplementation in pregnancy .[cochrane review], in the cochrane LIbrary, Issuel, Chichester, UK, John Wiley, 2004.

43. CLASP [collaborative Low- dose Aspirin Study in pregnancy] Collaborative Group. A randomised trial of low- dose aspirin for the preventive and treatment of pre-eclampsia in pregnant women. Lancet 1994;343 : 619-629.

44. Hofmeyr GJ, et al. Calcium supplementation to prevent pre-eclampsia a systematic review. South Afr Med J 2003;93:224-228.

45. Jane A Bates et al Differentiation of growth retarded from normally grown foetuses and prediction of intrauterine growth retardation using Doppler ultrasound BJOG 1996 ;103(7) ;670-675

46. Chudleigh T., Thilaganathan, Obstetric ultrasound how ,why and when,3rd , london Elsevier, B.2004;109)

47. Vicenzini, E., Giannoni, M. F., Ricciardi, M. C., Toscano, M., Sirimarco, G., Di Piero, V. and Lenzi, G. L. (2010), Noninvasive Imaging of Carotid Arteries in Stroke. Journal of Ultrasound in Medicine, 29: 1635–1641.

48. Doppler in Obstetrics.2002, by fetal medicine foundation .Kypros Nicholaides, Giuseppe Rizzo, Kurt Hetcher and Renato xemenes .p22

49. ISUOG practice guidelines2013.Ultrasound Obstet Gynaecol 2013; 41; 233-239

50. Kingdom JC, Burrell SJ, Kaufmann P. Pathology and clinical implications of abnormal umbilical artery Doppler waveforms. Ultrasound Obstet Gynecol 1997;9:271-86. Level III.

51. Morrow RJ, Adamson SL, Bull SB, Ritchie JW. Effect of placental embolization on the umbilical artery velocity waveform in fetal sheep. Am J Obstet Gynecol 1989;161:1055-60. Level III.

52. McIntire DD, Bloom SL, Casey BM, Leveno KJ. Birth weight in relation to morbidity and mortality among newborn infants. N Engl J Med 1999;340:1234-8. Level II-2.

53. Copel JA, Reed KL. Doppler ultrasound in obstetrics and gynecology, 1st ed. New York, NY: Raven Press; 1995:187–98. Level III.

54. Veille JC, Hanson R, Tatum K. Longitudinal quantitation of middle cerebral artery blood flow in normal human fetuses. Am J Obstet Gynecol 1993;169:1393-8. Level II-3.

55. Mari G, Hanif F, Kruger M, Cosmi E, Santolaya- Forgas J, Teadwell MC. Middle cerebral artery peak systolic velocity: a new Doppler parameter in the assessment of growth-restricted fetuses. Ultrasound Obstet Gynecol 2007;29: 310-6. Level II-3.

56. Kurmanavicius J, Florio I, Wisser J, et al. Reference resistance indices of the umbilical, fetal middle cerebral and uterine arteries at 24-42 weeks of gestation. Ultrasound Obstet Gynecol 1997; 10:112-20. Level II-2.

57. Behrman RE, Lees MH, Peterson EN, De Lannoy CW, Seeds AE. Distribution of the circulation in the normal and asphyxiated fetal primate.AmJ Obstet Gynecol 1970; 108:956-69. Level II-3.

58. Baschat AA, Hecher K. Fetal growth restriction due to placental disease. Semin Perinatol 2004; 28:67-80. Level III.

59.. Baschat AA. Fetal responses to placental insufficiency: an update. BJOG 2004; 111: 1031-41. Level III.

60. **25.** Jurkovic D, Jauniaux E, Kurjak A, et al. Transvaginal color Doppler assessment of the uteroplacental circulation in early pregnancy. Obstet Gynecol 1991; 77:365-9. Level II-3.

61. Jauniaux E, Jurkovic D, Campbell S, et al. Doppler ultrasonographic features of the developing placental circulation; correlation with anatomic findings. Am J Obstet Gynecol 1992; 166:585-7. Level II-3.

62. Papageorghiou AT, Yu CKH, Nicolaides KH. The role of uterine artery Doppler in predicting adverse pregnancy outcome. Best Pract Res Clin Obstet Gynecol 2004;18:383-96. Level III.

63. Papageorghiou AT, To MS, Yu CK, Nicolaides KH. Repeatability of measurement of uterine artery pulsatility index using transvaginal color Doppler. Ultrasound Obstet Gynecol 2001;18:456-9. Level II-3.

64. Cnossen J, Morris R, Riet G, et al. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction a systematic review and bivariable meta-analysis. CMAJ 2008;178:701-11. Level I.

65. Campbell S, Diaz-Recasens J, Griffin DR, et al. New Doppler technique for assessing uteroplacental blood flow. Lancet 1983;26:675-7.

66. Sciscione AC, Hayes EJ. Society for Maternal-Fetal Medicine: uterine artery Doppler flow studies in obstetric practice. Am J Obstet Gynecol 2009;201:121-6. Level III.

67. BASCHAT, A. A. & GEMBRUCH, U. 2003. The cerebroplacental Doppler ratio revisited. Ultrasound Obstet Gynecol, 21, 124-7.

68. DUBIEL, M., BREBOROWICZ, G. H., MARSAL, K. & GUDMUNDSSON, S. 2000. Fetal adrenal and middle cerebral artery Doppler velocimetry in high-risk pregnancy. *Ultrasound Obstet Gynecol,* 16**,** 414-

69. ARDUINI, D. & RIZZO, G. 1993. Doppler studies of deteriorating growth-retarded fetuses. *Curr Opin Obstet Gynecol,* 5**,** 195-203.

70. BAHLMANN, F., REINHARD, I., KRUMMENAUER, F., NEUBERT, S., MACCHIELLA, D. & WELLEK, S. 2002. Blood flow velocity waveforms of the fetal middle cerebral artery in a normal population: reference values from 18 weeks to 42 weeks of gestation. *J Perinat Med,* 30**,** 490-501.

71. MARI, G., MOISE, K. J., JR., DETER, R. L., KIRSHON, B., CARPENTER, R. J., JR. & HUHTA, J. C. 1989. Doppler assessment of the pulsatility index in the cerebral circulation of the human fetus. *Am J Obstet Gynecol,* 160**,** 698-703.

72. MANNING, F. A., PLATT, L. D. & SIPOS, L. 1980. Antepartum fetal evaluation: development of a fetal biophysical profile. *Am J Obstet Gynecol,* 136**,** 787-95.

73. WELLEK, S. & MERZ, E. 1995. Age-related reference ranges for growth parameters. *Methods Inf Med,* 34**,** 523-8.

74. Becker R, Vonk R, Vollert W, Entezami M. Doppler sonography of uterine arteries at 20-23 weeks: risk assessment of adverse pregnancy outcome by quantification of impedance and notch. J Perinat Med 2002;30(5):388-94.

75. Barati M, Shahbazian N, Ahmadi L, Masihi S. Diagnostic evaluation of uterine artery Doppler sonography for the prediction of adverse pregnancy outcomes. Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences. 2014;19(6):515-519.

76. Antsaklis A, Daskalakis G, Tzortzis E, Michalas S. The effect of gestational age with placental location on the prediction of pre-eclampsia. Uterine artery Doppler velocimetry in low risk nulliparous women. Obstet Gynecol. 2000; 16:635–639

77. Beattie RB, Dornan JC Antenatal screening for intrauterine growth retardation with umbilical artery Doppler ultrasonography. BMJ 1989 Mar 11; 298(6674):631-5

78.Romero Arauz JF, Ramos León JC, Rivera Velásquez P, Álvarez Jiménez G, Molina Pérez CJ.Umbilical artery Doppler velocimetry and adverse perinatal outcome in severe pre-eclampsia. . Ginecol Obstet Mex. 2008 Aug; 76(8):440-9.

79. Khanduri S, Parashari UC, Bashir S, Bhadury S, Bansal A. Comparison of Diagnostic Efficacy of Umbilical Artery and Middle Cerebral Artery Waveform with Color Doppler Study for Detection of Intrauterine Growth Restriction. Journal of Obstetrics and Gynaecology of India. 2013; 63(4):249-255.

80. A.A. BaschatPathophysiology of fetal growth restriction: implications for diagnosis and surveillance Obstet Gynecol Surv, 59 (2004), pp. 617-627

81. A.A. Baschat, U. Gembruch, C.P. Weiner, C.R. HarmanQualitative venous Doppler waveform analysis improves prediction of critical perinatal outcomes in premature growth restricted foetuses Ultrasound Obstet Gynecol, 22 (2003), pp. 240-245

82. A. Schwarze, U. Gembruch, M. Krapp, A. Katalinic, U. Germer, R. Axt-FliednerQualitative venous Doppler flow waveform analysis in preterm intrauterine growth restricted fetuses with ARED flow in the umbilical artery – correlation with short term outcome Ultrasound Obstet Gynecol (2005), pp. 573-579

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Case Report Form

Name:

Age / Sex

GA

Weight:

Height:

Parity:

Foetal Maternal Doppler

Uterine arteries

Pulsatility Index:

Diastolic Notch:

Umblical Artery

End diastolic flow:

Middle cerebral artery

Pulsatility index:

Ductus venosus

Wave form:

Follow up

Mother:

Gestational age at delivery: _____ weeks

Term/Preterm:

PIH/Pre-eclampsia

Baby:

Birth weight:

IUGR/SGA:

Admission in NICU:

If Yes, No of days stay:

Steroid requirement:

S.NO	NAME	AGE	GEST AGE AT SCAN	GRAVIDA	DIASTOLIC NOTCH	PI Uterine artery	UMBLICAL ARTERY - EDF	MCA - PI < 1.7	DUCTUS VENOSUS WAVE FORM	GEST AGE AT DELIVERY	TERM/ PRETERM	PRE ECLAMPSIA/ ECLAMPSIA	SGA/IUGR	BABY WT	NEONATAL ADMISSION REQUIRED	STEROID REQUIRED	DURATION OF NICU
1	VANITHA	22	22	1	Y	1.52	ABNORMAL	LOW	ABNORMAL	32	PRE	Y	Y	1.8	YES	YES	10
2	BAGYALAKSHMI	24	21	2	Y	1.65	ABNORMAL	NORMAL	ABNORMAL	33	PRE	Y	Y	2.1	YES	YES	10
3	GEETHA	27	20	3	N	1.23	NORMAL	NORMAL	NORMAL	37	TERM	N	N	2.9	NO	NO	0
4	PUNITHA	29	22	1	N	1.66	NORMAL	LOW	NORMAL	34	PRE	Y	Y	2	YES	YES	7
5	VADIVAMBAL	27	20	2	Y	1.07	NORMAL	LOW	NORMAL	38	TERM	N	N	2.9	NO	NO	0
6	NITHYA	20	21	1	N	1.81	NORMAL	NORMAL	NORMAL	38	TERM	N	N	2.8	NO	NO	0
7	REVATHY	32	22	2	N	1.08	ABNORMAL	NORMAL	NORMAL	34	PRE	Y	Y	2.1	YES	NO	8
8	VALLI	27	22	3	Y	1.52	ABNORMAL	LOW	ABNORMAL	37	TERM	N	N	2.8	NO	NO	0
9	KAVITHA	21	21	2	N	1.04	NORMAL	LOW	ABNORMAL	39	TERM	N	N	2.7	NO	NO	0
10	SRIVIDYA	34	20	1	Y	1.52	ABNORMAL	NORMAL	ABNORMAL	32	PRE	Y	Y	1.9	YES	YES	18
11	SANGEETHA	31	20	3	N	1.28	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.5	NO	NO	0
12	RAJALAKSHMI	25	21	2	N	1.3	NORMAL	NORMAL	NORMAL	40	TERM	N	N	2.7	NO	NO	0
13	JAYASUDHA	24	20	2	N	1.3	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.8	NO	NO	0
14	POORNIMA	26	22	2	Y	1.65	ABNORMAL	LOW	ABNORMAL	32	PRE	N	Y	1.8	YES	NO	10
15	SUNDHARI	27	20	2	N	1.32	NORMAL	NORMAL	NORMAL	40	TERM	N	N	2.9	NO	NO	0
16	AYESHA	35	22	3	N	1.33	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.8	NO	NO	0
17	FOUZIYA	34	22	2	N	1.32	NORMAL	NORMAL	NORMAL	38	TERM	N	N	3.1	NO	NO	0
18	SANTHA	28	21	1	Y	1.7	ABNORMAL	LOW	NORMAL	31	PRE	Y	Y	2	YES	NO	11
19	VIJAYA	27	21	2	Y	1.36	NORMAL	LOW	ABNORMAL	38	TERM	Y	Y	2.1	YES	YES	9
20	GOVINDHAMMAL	19	22	1	N	1.3	NORMAL	LOW	ABNORMAL	38	TERM	Y	Y	1.9	NO	NO	0
21	RANI	21	20	1	N	1.26	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.8	NO	NO	0
22	SUSHILA	23	21	2	N	1.3	NORMAL	NORMAL	NORMAL	37	TERM	N	N	2.9	NO	YES	0
23	ELAVARASI	25	20	1	N	1.4	NORMAL	NORMAL	NORMAL	39	TERM	N	N	3.2	NO	NO	0
24	VIJAYALAKSHMI	27	21	1	Y	1.32	ABNORMAL	LOW	ABNORMAL	30	PRE	N	Y	1.6	YES	YES	8

25	GEETHA	21	22	2	N	1.41	NORMAL	NORMAL	NORMAL	38	TERM	N	N	3.3	NO	NO	0
26	MADURA	26	20	2	N	1.34	ABNORMAL	NORMAL	ABNORMAL	38	TERM	N	N	3.5	NO	NO	0
27	LILLY	19	20	1	N	1.33	NORMAL	NORMAL	NORMAL	39	TERM	N	Y	2.2	NO	NO	0
28	ABITHA	30	20	3	N	1.18	NORMAL	NORMAL	NORMAL	37	TERM	N	N	3.2	NO	NO	0
29	KALAIARASI	31	22	2	Y	1.53	ABNORMAL	LOW	ABNORMAL	32	PRE	Y	Y	2.1	YES	YES	8
30	SUDHA	35	21	1	N	1.37	NORMAL	NORMAL	NORMAL	38	TERM	N	N	2.9	NO	NO	0
31	KEERTHANA	29	20	2	N	1.34	NORMAL	LOW	NORMAL	32	PRE	Y	Y	1.8	NO	NO	0
32	UMA	25	21	2	N	1.53	ABNORMAL	NORMAL	NORMAL	32	PRE	N	N	2.6	YES	NO	5
33	YAMUNA RANI	24	22	1	N	1.35	NORMAL	NORMAL	NORMAL	39	TERM	N	N	3.1	NO	NO	0
34	MALAR	26	22	1	N	1.5	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.9	NO	NO	0
35	BHUVANESHWARI	27	20	2	Y	1.36	ABNORMAL	NORMAL	ABNORMAL	38	TERM	Y	N	2.9	NO	NO	0
36	SASIKALA	22	20	1	N	1.45	NORMAL	NORMAL	NORMAL	38	TERM	N	N	3.1	NO	NO	0
37	PRIYA	21	21	1	N	1.38	NORMAL	NORMAL	NORMAL	39	TERM	N	N	3	NO	NO	0
38	CHITRA	24	21	2	N	1.42	NORMAL	NORMAL	NORMAL	39	TERM	N	N	3.1	NO	NO	0
39	RADHA	23	21	1	N	1.55	NORMAL	LOW	ABNORMAL	32	PRE	Y	Y	1.9	YES	NO	6
40	KALA	28	22	2	Y	1.68	ABNORMAL	LOW	NORMAL	33	PRE	N	Y	2.1	YES	YES	13
41	SELVI	22	20	1	N	1.3	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.9	NO	NO	0
42	DHANAM	24	21	1	N	1.27	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.8	NO	NO	0
43	GAJALAKSHMI	20	20	1	N	1.26	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.5	NO	NO	0
44	JAMUNA	19	21	1	N	1.4	NORMAL	NORMAL	ABNORMAL	38	TERM	N	N	2.7	NO	NO	0
45	ESWARI	23	21	1	N	1.6	NORMAL	NORMAL	NORMAL	39	TERM	N	Y	2.1	NO	NO	0
46	PRABHA	25	20	1	N	1.43	NORMAL	NORMAL	NORMAL	38	TERM	N	N	2.6	NO	NO	0
47	GAYATHRI	26	22	2	Y	1.17	NORMAL	NORMAL	NORMAL	38	TERM	N	N	2.9	NO	NO	0
48	MUNIAMMAL	24	22	1	N	1.5	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.9	NO	NO	0
49	PAVITHRA	25	21	1	N	1.54	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.6	NO	NO	0
50	ELAYARANI	29	20	2	N	1.42	NORMAL	NORMAL	NORMAL	39	TERM	N	N	2.7	NO	NO	0